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STRUCTURE FILE UPDATES: 29 AUG 2006 HIGHEST RN 905300-98-3
DICTIONARY FILE UPDATES: 29 AUG 2006 HIGHEST RN 905300-98-3

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STRUCTURE
QUERIES

=> d stat que L9
L1 STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.

L3	304	SEA	FILE=REGISTRY	SSS	FUL	L1
L5	283	SEA	FILE=REGISTRY	ABB=ON	PLU=ON	RGDFK/SQEP
L6	72	SEA	FILE=REGISTRY	ABB=ON	PLU=ON	RGDYK/SQEP
L7	29659	SEA	FILE=REGISTRY	ABB=ON	PLU=ON	CYCLIC/NTE
L8	333	SEA	FILE=REGISTRY	ABB=ON	PLU=ON	(L5 OR L6) AND L7
L9	338	SEA	FILE=REGISTRY	ABB=ON	PLU=ON	L3 OR L8

=> d stat que L12
L12 1 SEA FILE=REGISTRY ABB=ON PLU=ON KLAKKLAK/SQEP

=> d stat que L33
L33 98 SEA FILE=REGISTRY ABB=ON PLU=ON KLAKKLAK/SQSP

=> d sqide L12

L12 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2006 ACS on STN
RN 615263-22-4 REGISTRY
CN L-Lysine, L-lysyl-L-leucyl-L-alanyl-L-lysyl-L-lysyl-L-leucyl-L-alanyl-
(9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE; STEREOSEARCH
SQL 8

SEQ 1 KLAKKLAK

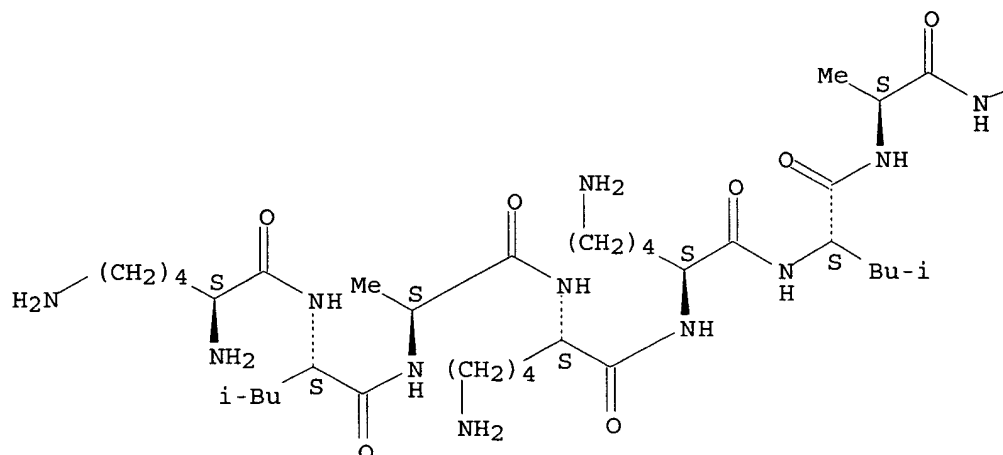
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HITS AT: 1-8

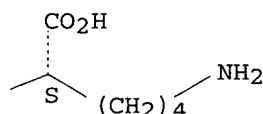
MF C42 H82 N12 O9
 SR CA
 LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL
 DT.CA Caplus document type: Patent
 RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

- 1 REFERENCES IN FILE CA (1907 TO DATE)
- 1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
- 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

AUTHOR
SEARCH

=> => file hcaplus
 FILE 'HCAPLUS' ENTERED AT 15:16:15 ON 30 AUG 2006
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FILE COVERS 1907 - 30 Aug 2006 VOL 145 ISS 10
FILE LAST UPDATED: 29 Aug 2006 (20060829/ED)

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This file contains CAS Registry Numbers for easy and accurate substance identification.

'OBI' IS DEFAULT SEARCH FIELD FOR 'HCAPLUS' FILE

=> d que nos L44

L37	116	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	DUMY P?/AU
L38	47	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	FAVROT M?/AU
L39	20	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	BOTURYN D?/AU
L40	459	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	COLL J?/AU
L41	14	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	L37 AND (L38 OR L39 OR L40)
L42	21	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	L38 AND (L39 OR L40)
L43	5	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	L39 AND L40
L44	30	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	(L41 OR L42 OR L43)

author search

=> d que nos L45

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L5	283	SEA	FILE=REGISTRY	ABB=ON	PLU=ON	RGDFK/SQEP
L6	72	SEA	FILE=REGISTRY	ABB=ON	PLU=ON	RGDYK/SQEP
L7	29659	SEA	FILE=REGISTRY	ABB=ON	PLU=ON	CYCLIC/NTE
L8	333	SEA	FILE=REGISTRY	ABB=ON	PLU=ON	(L5 OR L6) AND L7
L9	338	SEA	FILE=REGISTRY	ABB=ON	PLU=ON	L3 OR L8
L11	120	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	L9
L12	1	SEA	FILE=REGISTRY	ABB=ON	PLU=ON	KLAKKLAK/SQEP
L13	1	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	L12
L17	35926	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	?INTEGRIN?/BI
L18	15515	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	?DOXORUBICIN?/BI
L19	151236	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	?GRAFT?/BI
L20	81	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	L11 AND L17
L21	7	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	L11 AND L17 AND L18
L22	21	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	L11 AND L19
L28	275948	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	?OXIM?/BI
L29	13	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	L11 AND L28
L30	11	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	L11 AND L18
L31	42	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	(L13 OR L21 OR L22 OR L29 OR L30)
L32	29	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	(L13 OR L21 OR L22 OR L29 OR L30) AND L20
L33	98	SEA	FILE=REGISTRY	ABB=ON	PLU=ON	KLAKKLAK/SQSP
L34	85	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	L33
L36	6	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	L34 AND L19
L37	116	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	DUMY P?/AU
L38	47	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	FAVROT M?/AU
L39	20	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	BOTURYN D?/AU
L40	459	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	COLL J?/AU
L41	14	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	L37 AND (L38 OR L39 OR L40)
L42	21	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	L38 AND (L39 OR L40)
L43	5	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	L39 AND L40
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L45 5 SEA FILE=HCAPLUS ABB=ON PLU=ON L44 AND (L31 OR L32 OR L36)

=> s L44-L45

L46 30 (L44 OR L45)

=> d ibib abs hitind hitrn hitstr L46 1-30

L46 ANSWER 1 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:814919 HCAPLUS

TITLE: Redox-Active Biomolecular Architectures and Self-Assembled Monolayers Based on a Cyclodecapeptide Regioselectively Addressable Functional Template

AUTHOR(S): Devillers, Charles H.; **Boturyn, Didier**; Bucher, Christophe; **Dumy, Pascal**; Labbe, Pierre; Moutet, Jean-Claude; Royal, Guy; Saint-Aman, Eric

CORPORATE SOURCE: Laboratoire d'Electrochimie Organique et de Photochimie Redox UMR CNRS 5630 Institut de Chimie Moleculaire de Grenoble, Universite Joseph Fourier, Grenoble, 38041, Fr.

SOURCE: Langmuir (2006), 22(19), 8134-8143

CODEN: LANGD5; ISSN: 0743-7463

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A nanometer scale redox active biomol. architecture has been successfully synthesized through an efficient chemoselective oxime based coupling between ferrocenyl groups and a regioselectively addressable cyclodecapeptide. This mol. tool exhibits electronic, structural, and chemical properties driven by the biomimetic recognition activity of the polypeptide skeleton associated to the well-defined electrochem. activity of metallocenyl probes. Biomol. materials obtained by confinement of the redox cyclopeptide in self-assembled monolayers on gold surfaces shows efficient through-bond electron transfer from the ferrocenes to the electrode surface via the peptidic backbone, as well as markedly improved sensing properties toward anionic species in organic electrolyte, as compared to those observed in homogeneous solution

CC 9 (Biochemical Methods)

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L46 ANSWER 2 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:550255 HCAPLUS

TITLE: Model Peptides Based on the Binding Loop of the Copper Metallochaperone Atx1: Selectivity of the Consensus Sequence MxCxxC for Metal Ions Hg(II), Cu(I), Cd(II), Pb(II), and Zn(II)

AUTHOR(S): Rousselot-Pailley, Pierre; Seneque, Olivier; Lebrun, Colette; Crouzy, Serge; **Boturyn, Didier**; **Dumy, Pascal**; Ferrand, Michel; Delangle, Pascale

CORPORATE SOURCE: Laboratoire de Reconnaissance Ionique, DRFMC/LCIB (UMR_E 3 CEA-UJF), CEA-Grenoble, Grenoble, F-38054, Fr.

SOURCE: Inorganic Chemistry (2006), 45(14), 5510-5520

CODEN: INOCAJ; ISSN: 0020-1669

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The amino acid sequence MxCxxC is conserved in many soft-metal transporters that are involved in the control of the intracellular concentration

of ions such as Cu(I), Hg(II), Zn(II), Cd(II), and Pb(II). A relevant task is thus the selectivity of the motif MxCxxC for these different metal ions. To analyze the coordination properties and the selectivity of this consensus sequence, we have designed two model peptides that mimic the binding loop of the copper chaperone Atx1: the cyclic peptide PC c(GMTCSGCSRPG) and its linear analog PL (Ac-MTCSGCSRPG-NH₂). By using complementary anal. and spectroscopic methods, we have demonstrated that 1:1 complexes are obtained with Cu(I) and Hg(II), whereas 1:1 and 1:2 (M:P) species are successively formed with Zn(II), Cd(II), and Pb(II). The complexation properties of the cyclic and linear peptides are very close, but the cyclic compound provides systematically higher affinity consts. than its unstructured analog. The introduction of a xPGx motif that forms a type II β turn in PC induces a preorganization of the binding loop of the peptide that enhances the stabilities of the complexes (up to 2 orders of magnitude difference for the Hg complexes). The affinity consts. were measured in the absence of any reducing agent that would compete with the peptides and range in the order Hg(II) > Cu(I) > Cd(II) > Pb(II) > Zn(II). This sequence is thus highly selective for Cu(I) compared to the essential ion Zn(II) that could compete in vivo or compared to the toxic ions Cd(II) and Pb(II). Only Hg(II) may be an efficient competitor of Cu(I) for binding to the MxCxxC motif in metalloproteins.

CC 6-3 (General Biochemistry)

REFERENCE COUNT: 80 THERE ARE 80 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L46 ANSWER 3 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:453992 HCAPLUS

DOCUMENT NUMBER: 145:167523

TITLE: Multivalent RGD synthetic peptides as potent α V β 3 integrin ligands

AUTHOR(S): Garanger, Elisabeth; Boturyn, Didier; Coll, Jean-Luc; Favrot, Marie-Christine; Dumy, Pascal

CORPORATE SOURCE: Ingenierie Moleculaire et Chimie Bioorganique, LEDSS, CNRS UMR 5616, ICMG FR 2607, Universite Joseph Fourier, Grenoble, 38041, Fr.

SOURCE: Organic & Biomolecular Chemistry (2006), 4(10), 1958-1965

CODEN: OBCRAK; ISSN: 1477-0520

PUBLISHER: Royal Society of Chemistry

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The multivalency effect of a cluster of α V β 3-ligands held on a cyclodecapeptide template has been studied. An array of RAFT(c[-RGDfK-])_n derivs. containing from one to sixteen clustered RGD motifs were synthesized and comparatively assayed in vitro on α V β 3-expressing cells. Efficient inhibition of the α V β 3-specific 23C6 monoclonal antibody fixation was observed with ligands displaying three and four copies of the cyclo[-RGDfK-] peptide.

CC 34-3 (Amino Acids, Peptides, and Proteins)

Section cross-reference(s): 1

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L46 ANSWER 4 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:324292 HCAPLUS
 DOCUMENT NUMBER: 144:365501
 TITLE: Use of VCAM-1 ligands for the detection and/or the treatment of cardiovascular diseases
 INVENTOR(S): **Boturyn, Didier**; Riou, Laurent; Ghezzi, Catherine; Fagret, Daniel; **Dumy, Pascal**
 PATENT ASSIGNEE(S): Inst. National de la Sante et de la Recherche Medicale Inserm, Fr.
 SOURCE: Fr. Demande, 30 pp.
 CODEN: FRXXBL
 DOCUMENT TYPE: Patent
 LANGUAGE: French
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2876033	A1	20060407	FR 2004-10420	20041001
WO 2006037882	A1	20060413	WO 2005-FR2423	20050930

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: FR 2004-10420 A 20041001

AB The invention discloses the use of ligands of VCAM-1 in medical imaging, in particular for characterization and/or therapeutic follow-up of cardiovascular diseases and more particularly for the detection of vulnerable coronary atheroma plaque. The invention also discloses the use of ligands of VCAM-1 for the manufacture of a drug intended for the treatment of a cardiovascular disease.

CC 8-9 (Radiation Biochemistry)
 Section cross-reference(s): 1

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L46 ANSWER 5 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:124024 HCAPLUS
 DOCUMENT NUMBER: 144:370403
 TITLE: Chemoselectively Addressable Template: A Valuable Tool for the Engineering of Molecular Conjugates
 AUTHOR(S): Garanger, Elisabeth; **Boturyn, Didier**; Renaudet, Olivier; Defrancq, Eric; **Dumy, Pascal**
 CORPORATE SOURCE: LEDSS, Grenoble, 38041, Fr.
 SOURCE: Journal of Organic Chemistry (2006), 71(6), 2402-2410
 CODEN: JOCEAH; ISSN: 0022-3263
 PUBLISHER: American Chemical Society
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 144:370403
 AB We report the modular design and the synthesis of new mol. conjugates, which can combine a cell targeting function (ligand domain) with potential

cytotoxic mols. (effector domain). The present approach utilizes a cyclic peptide template, Chemoselectively Addressable Template (CAT) as a key intermediate. These CAT mols. exhibit two independent and chemical addressable domains which permits the sequential and regioselective assembly of different ligand and/or effector domains. The attachment of various units to the template was achieved by the formation of iterative **oxime** bonds. The chemoselective **oxime** bonds were produced by the reaction of glyoxylyl aldehyde groups obtained from serine precursors. The process was further developed to prevent **transoximation** reactions. RAFT(c[-RGDfK-])₄, a synthetic vector targeting the tumor-associated α V β 3 **integrin** was prepared and coupled to either a cytotoxic peptide or oligonucleotide as an illustration of the present approach. The potential application of this approach has been further demonstrated by the synthesis of high mol. weight compds. such as RAFT(c[-RGDfK-])₁₆, a α V β 3-targeting ligand of high valency index.

CC 34-3 (Amino Acids, Peptides, and Proteins)

Section cross-reference(s): 33

IT Regiochemistry

(chemoselectively addressable template (CAT) in preparation of conjugate between synthetic vector targeting tumor-associated α V β 3 **integrin** and cytotoxic peptide or oligonucleotide)

IT Glycoconjugates

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(chemoselectively addressable template (CAT) in preparation of conjugate between synthetic vector targeting tumor-associated α V β 3 **integrin** and cytotoxic peptide or oligonucleotide)

IT Peptides, preparation

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)

(cyclic; chemoselectively addressable template (CAT) in preparation of conjugate between synthetic vector targeting tumor-associated α V β 3 **integrin** and cytotoxic peptide or oligonucleotide)

IT Oximation

(in preparation of conjugate between synthetic vector targeting tumor-associated α V β 3 **integrin** and cytotoxic peptide or oligonucleotide)

IT 882194-67-4P

RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)

(chemoselectively addressable template (CAT) in preparation of conjugate between synthetic vector targeting tumor-associated α V β 3 **integrin** and cytotoxic peptide or oligonucleotide)

IT 13734-38-8 80366-85-4 343312-27-6 882051-20-9 882051-21-0 882051-22-1

RL: RCT (Reactant); RACT (Reactant or reagent)

(chemoselectively addressable template (CAT) in preparation of conjugate between synthetic vector targeting tumor-associated α V β 3 **integrin** and cytotoxic peptide or oligonucleotide)

IT 163395-17-3P 343312-28-7P 499222-40-1P 499222-41-2P

696660-66-9P 859802-81-6P 882051-18-5P 882051-23-2P

882051-25-4P 882051-26-5P 882051-27-6P 882051-28-7P

882067-03-0P 882067-05-2P 882067-06-3P 882194-66-3P

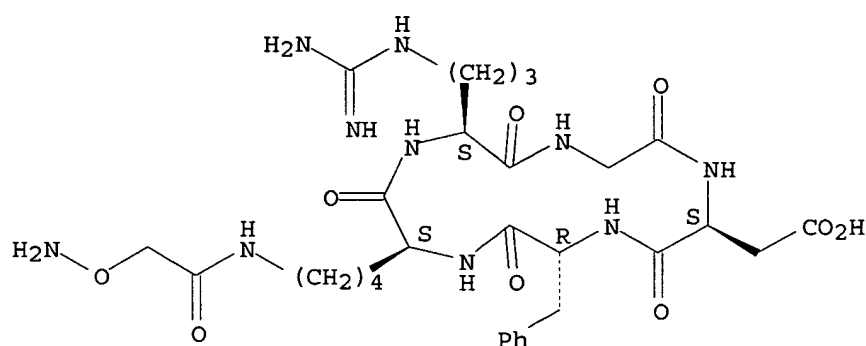
885070-42-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(chemoselectively addressable template (CAT) in preparation of conjugate between synthetic vector targeting tumor-associated α V β 3

integrin and cytotoxic peptide or oligonucleotide)
IT 882051-24-3P 882067-01-8P 882067-02-9P
882067-04-1P 882067-07-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(chemoselectively addressable template (CAT) in preparation of conjugate
between synthetic vector targeting tumor-associated $\alpha V\beta 3$
integrin and cytotoxic peptide or oligonucleotide)
IT 882194-65-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(hybridization; chemoselectively addressable template (CAT) in preparation
of conjugate between synthetic vector targeting tumor-associated
 $\alpha V\beta 3$ **integrin** and cytotoxic peptide or
oligonucleotide)
IT 29022-11-5, Fmoc-Gly-OH 71989-31-6 104091-09-0 150629-67-7
174653-61-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(selectively addressable template (CAT) in preparation of conjugate between
synthetic vector targeting tumor-associated $\alpha V\beta 3$
integrin and cytotoxic peptide or oligonucleotide)
IT 343312-27-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(chemoselectively addressable template (CAT) in preparation of conjugate
between synthetic vector targeting tumor-associated $\alpha V\beta 3$
integrin and cytotoxic peptide or oligonucleotide)
IT 343312-28-7P 882051-23-2P 882051-25-4P
882067-06-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(chemoselectively addressable template (CAT) in preparation of conjugate
between synthetic vector targeting tumor-associated $\alpha V\beta 3$
integrin and cytotoxic peptide or oligonucleotide)
IT 882051-24-3P 882067-01-8P 882067-02-9P
882067-04-1P 882067-07-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(chemoselectively addressable template (CAT) in preparation of conjugate
between synthetic vector targeting tumor-associated $\alpha V\beta 3$
integrin and cytotoxic peptide or oligonucleotide)
IT 343312-27-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(chemoselectively addressable template (CAT) in preparation of conjugate
between synthetic vector targeting tumor-associated $\alpha V\beta 3$
integrin and cytotoxic peptide or oligonucleotide)
RN 343312-27-6 HCAPLUS
CN Cyclo[L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-N6-
[(aminooxy)acetyl]-L-lysyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 343312-28-7P 882051-23-2P 882051-25-4P
882067-06-3P

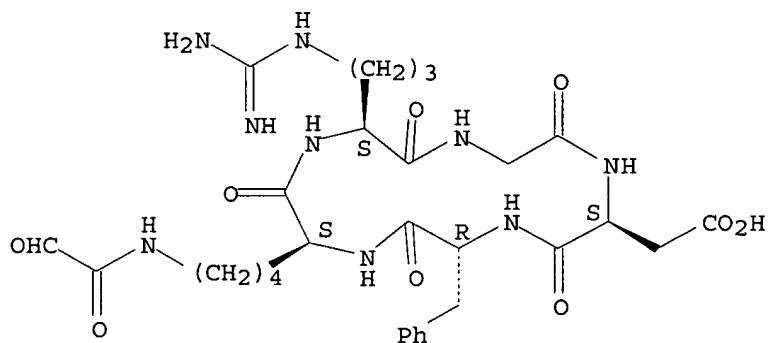
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)

(chemoselectively addressable template (CAT) in preparation of conjugate
between synthetic vector targeting tumor-associated $\alpha V\beta 3$
integrin and cytotoxic peptide or oligonucleotide)

RN 343312-28-7 HCAPLUS

CN Cyclo[L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-N6-(oxoacetyl)-L-
lysyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.

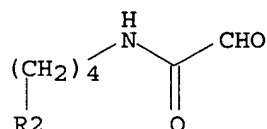
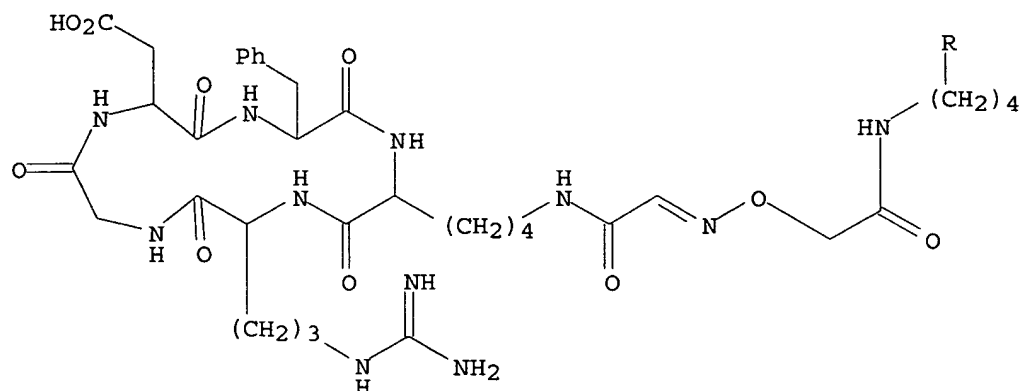


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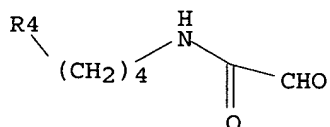
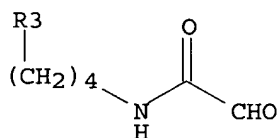
CN Cyclo[glycyl-N6-(oxoacetyl)-L-lysyl-N6-[(aminooxy)acetyl]-L-lysyl-N6-
(oxoacetyl)-L-lysyl-L-prolylglycyl-N6-(oxoacetyl)-L-lysyl-N6-
[(aminooxy)acetyl]-L-lysyl-N6-(oxoacetyl)-L-lysyl-L-prolyl],
(5'→3), (5'→8)-dialdoxime with cyclo[L-arginylglycyl-L-
 α -aspartyl-D-phenylalanyl-N6-(oxoacetyl)-L-lysyl] (9CI) (CA INDEX
NAME)

O=C(NCCCCNC(=O)CCNC(=O)C(R)NC(=O)C(R3)NC(=O)CCNC(=O)C(R2)N1CCCCC1)C(R4)NC(=O)N2CCCC2C(=O)N2CCCCC2C(=O)C(R)NC(=O)C(R3)NC(=O)CCNC(=O)C(R2)N1CCCCC1[illegible]

PAGE 2-A



PAGE 3-A

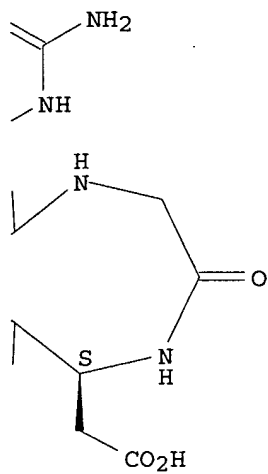


RN 882051-25-4 HCAPLUS

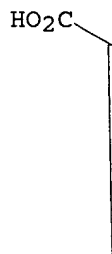
CN Cyclo[D-glutaminy1-N6-(oxoacetyl)-L-lysyl-N6-[(aminooxy)acetyl]-L-lysyl-N6-(oxoacetyl)-L-lysyl-L-prolylglycyl-N6-(oxoacetyl)-L-lysyl-N6-[(aminooxy)acetyl]-L-lysyl-N6-(oxoacetyl)-L-lysyl-L-prolyl], (5'→3), (5'→8)-dialdoxime with cyclo[L-arginylglycyl-L-α-aspartyl-D-phenylalanyl-N6-(oxoacetyl)-L-lysyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

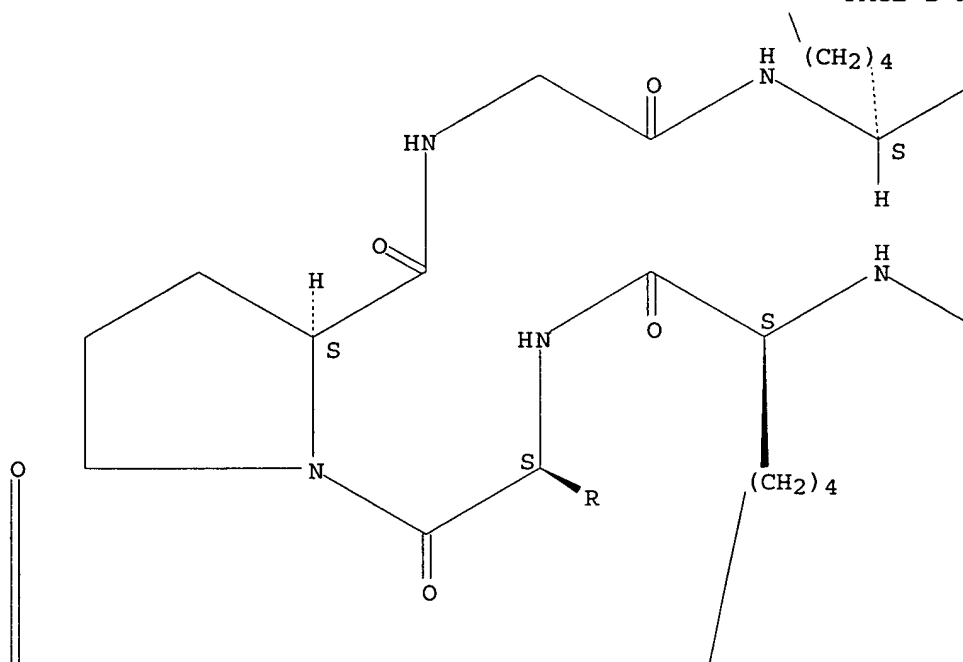
PAGE 1-D



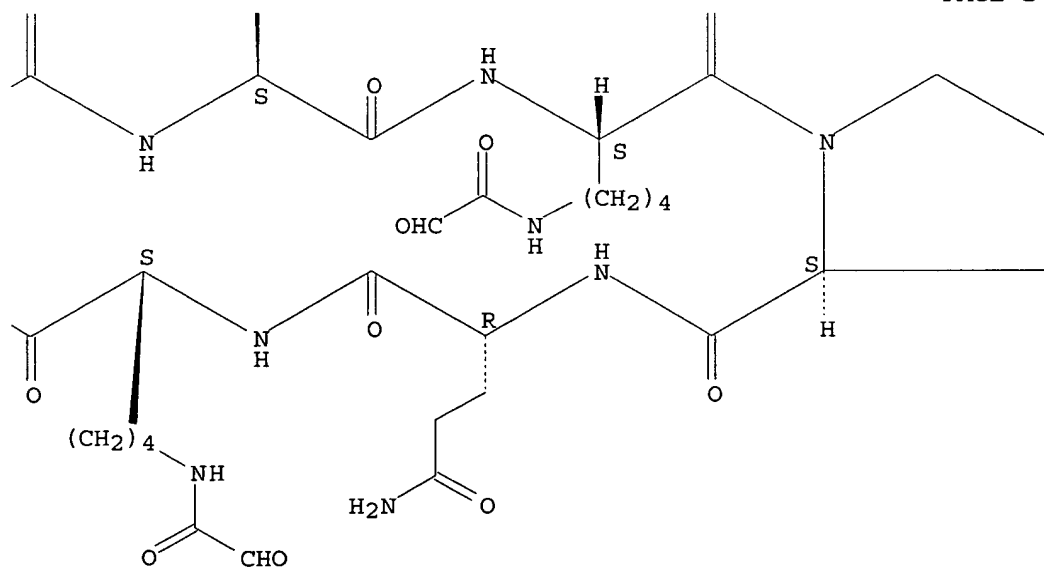
PAGE 2-A



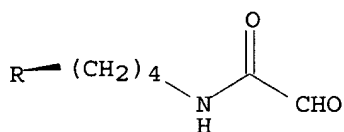
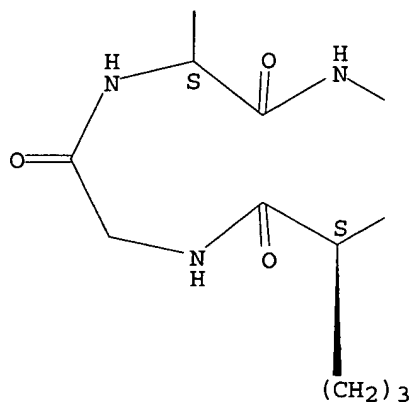
PAGE 2-B



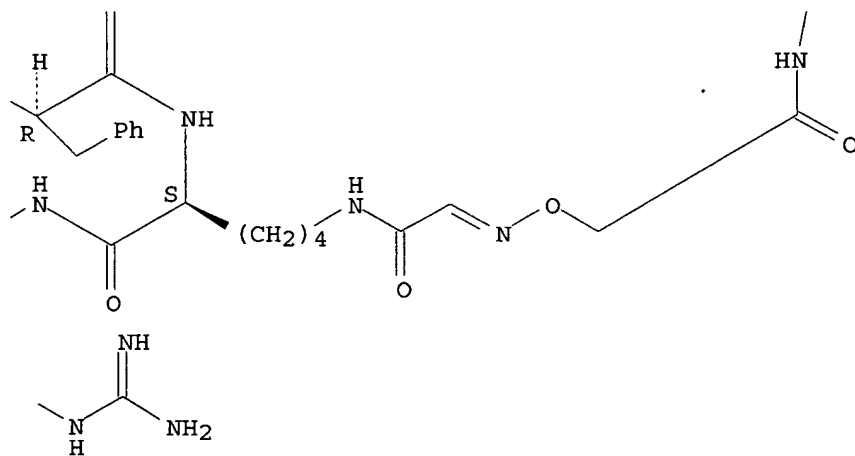
PAGE 2-C



PAGE 3-A



PAGE 3-B



RN 882067-06-3 HCAPLUS

CN Cyclo[L-alanyl-N6-[(aminooxy)acetyl]-L-lysyl-L-prolylglycyl-N6-[(aminooxy)acetyl]-L-lysyl-N6-(oxoacetyl)-L-lysyl-N6-[(aminooxy)acetyl]-L-lysyl-L-prolylglycyl-N6-[(aminooxy)acetyl]-L-lysyl], (5'→2), (5'→5), (5'→7), (5'→10)-tetraaldoxime with cyclo[L-arginylglycyl-L-α-aspartyl-D-phenylalanyl-N6-(oxoacetyl)-L-lysyl] (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT 882051-24-3P 882067-01-8P 882067-02-9P

882067-04-1P 882067-07-4P

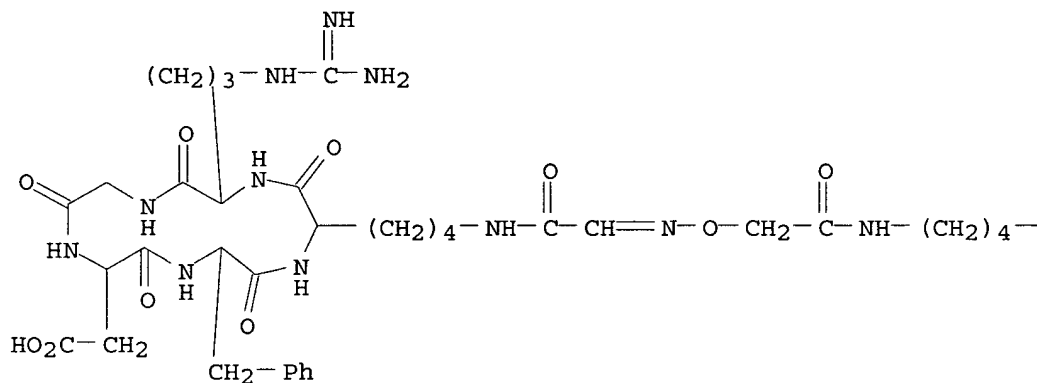
RL: SPN (Synthetic preparation); PREP (Preparation)

(chemoselectively addressable template (CAT) in preparation of conjugate between synthetic vector targeting tumor-associated $\alpha\text{V}\beta 3$ integrin and cytotoxic peptide or oligonucleotide)

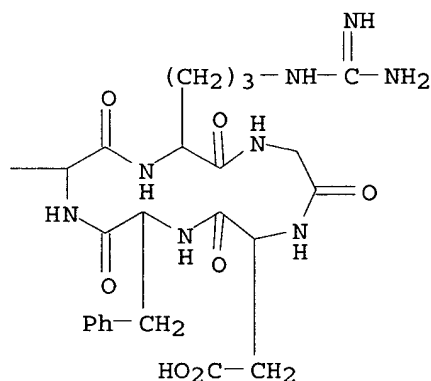
RN 882051-24-3 HCAPLUS

CN Cyclo[L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-N6-(oxoacetyl)-L-lysyl], (5 \rightarrow 5')-aldoxime with cyclo[L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-N6-[(aminooxy)acetyl]-L-lysyl] (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



RN 882067-01-8 HCAPLUS

CN Cyclo[glycyl-N6-(oxoacetyl)-L-lysyl-N6-[(aminooxy)acetyl]-L-lysyl-N6-(oxoacetyl)-L-lysyl-L-prolylglycyl-N6-(oxoacetyl)-L-lysyl-N6-[(aminooxy)acetyl]-L-lysyl-N6-(oxoacetyl)-L-lysyl-L-prolyl], (5' \rightarrow 3'), (5' \rightarrow 8)-dialdoxime with cyclo[L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-N6-(oxoacetyl)-L-lysyl], (2 \rightarrow 5'''), (4 \rightarrow 5'''), (7 \rightarrow 5'''), (9 \rightarrow 5''')-tetraaldoxime with cyclo[L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-N6-[(aminooxy)acetyl]-L-lysyl] (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

```

RN      882067-02-9   HCAPLUS
CN      Cyclo[D-glutaminy]l-N6-(oxoacetyl)-L-lysyl-N6-[(aminooxy)acetyl]-L-lysyl-N6-
        (oxoacetyl)-L-lysyl-L-prolylglycyl-N6-(oxoacetyl)-L-lysyl-N6-
        [(aminooxy)acetyl]-L-lysyl-N6-(oxoacetyl)-L-lysyl-L-prolyl],
        (5'→3), (5'→8)-dialdoxime with cyclo[L-arginylglycyl-L-
        α-aspartyl-D-phenylalanyl-N6-(oxoacetyl)-L-lysyl],
        (2→5'''), (4→5'''), (7→5'''), (9→5''')-
        tetraaldoxime with cyclo[L-arginylglycyl-L-α-aspartyl-D-phenylalanyl-
        N6-[(aminooxy)acetyl]-L-lysyl] (9CI) (CA INDEX NAME)

```

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 882067-04-1 HCAPLUS
CN L-Lysine, N-(oxoacetyl)glycylglycyl-L-lysyl-L-leucyl-L-alanyl-L-lysyl-L-leucyl-L-alanyl-L-lysyl-L-lysyl-L-leucyl-L-alanyl-L-lysyl-L-leucyl-L-alanyl-, (1→3''), (1'→8'')-dialdoxime with cyclo[glycyl-N6-(oxoacetyl)-L-lysyl-N6-[(aminooxy)acetyl]-L-lysyl-N6-(oxoacetyl)-L-lysyl-L-prolylglycyl-N6-(oxoacetyl)-L-lysyl-N6-[(aminooxy)acetyl]-L-lysyl-N6-(oxoacetyl)-L-lysyl-L-prolyl] (2'→5'''), (4'→5'''), (7'→5'''), (9'→5'')-tetraaldoxime with cyclo[L-arginylglycyl-L-α-aspartyl-D-phenylalanyl-N6-[(aminooxy)acetyl]-L-lysyl] (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

```

RN      882067-07-4      HCAPLUS
CN      Cyclo[L-alanyl-N6-(oxoacetyl)-L-lysyl-L-prolylglycyl-N6-(oxoacetyl)-L-
        lysyl-L-alanyl-N6-(oxoacetyl)-L-lysyl-L-prolylglycyl-N6-(oxoacetyl)-L-
        lysyl], (2→4'), (5→4'''), (7→4'''''), (10→4''''''')
        ')-tetraaldoxime with N2,N6-bis[N2,N6-bis(oxoacetyl)-L-lysyl]-L-lysyl-L-
        tyrosyl-N6-[(aminooxy)acetyl]-L-lysine (1'→5'''''''''), (1'→5
        '''''''), (1''→5'''''''), (1''→5'''''''''), (1'''→5''''''''')
        arw.5'''''''''), (1'''→5'''''''''), (1''''→5'''''''''), (1''''→5''''''''
        '''''''), (1''''→5'''''''''), (1''''→5'''''''''), (1''''→5''''''''
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        '''''''), (1''''→5'''''''''), (1''''→5'''''''''), (1''''→5''''''
        '''''''), (1''''→5'''''''''), (1''''→5''''''''') -
        hexadecaaldoxime with cyclo[L-arginylglycyl-L-α-aspartyl-D-
        phenylalanyl-N6-[(aminooxy)acetyl]-L-lysyl] (9CI) (CA INDEX NAME)

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*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L46 ANSWER 6 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1252336 HCAPLUS

DOCUMENT NUMBER: 144:156355

TITLE: New Multifunctional Molecular Conjugate Vector for
Targeting, Imaging, and Therapy of Tumors

AUTHOR(S) : Garanger, Elisabeth; Boturyn, Didier; Jin,
Zhaohui; Dumy, Pascal; Favrot,
Marie-Christine; Coll, Jean-Luc

CORPORATE SOURCE: Groupe de Recherche sur le Cancer du Poumon, INSERM
U578, Institut Albert Bonniot, La Tronche, 38706, Fr.

SOURCE: Molecular Therapy (2005), 12(6), 1168-1175

CODEN: MTOHCK; ISSN: 1525-0016

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal

LANGUAGE: English

AB We report the in vitro and in vivo characteristics of a new mol. conjugate vector for targeting and imaging of tumors. Its core is a

cyclodecapeptide platform named RAFT, onto which two spatially independent functional domains can be covalently and stereospecifically linked: a cell-targeting domain for tumor targeting and a labeling domain able to carry two drugs and/or labeling agents. To prove the interest of this carrier, we used a well-known cRGD cyclopeptide, a ligand for the $\alpha v \beta 3$ integrin. We demonstrate that this vector presenting four cRGD motifs very efficiently prevents $\alpha v \beta 3$ -mediated cell adhesion to vitronectin. Furthermore, it is actively endocytosed because of the multivalent cRGD presentation, a major advantage for drug delivery. In vivo expts. in nude mice reveal that repeated intratumoral injections of low doses of RAFT(cRGD)₄ reduce tumor growth. Furthermore, RAFT(cRGD)₄ significantly improves the targeting specificity of s.c. tumor masses as well as that of disseminated metastasis after i.v. injection. Thus, RAFT(cRGD)₄ is specific, internalized, and perfectly controlled and can carry multiple biol. functions on a single, spatially defined backbone, making it a powerful and versatile synthetic vector for drug delivery, mol. imaging, or both.

CC 63-5 (Pharmaceuticals)

Section cross-reference(s): 1

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L46 ANSWER 7 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:862911 HCAPLUS

DOCUMENT NUMBER: 144:376180

TITLE: Poor intercellular transport and absence of enhanced antiproliferative activity after non-viral gene transfer of VP22-P53 or P53-VP22 fusions into p53 null cell lines in vitro or in vivo

AUTHOR(S): Zavaglia, David; Lin, Erh-Hsuan; Guidetti, Melanie; Pluquet, Olivier; Hainaut, Pierre; Favrot, Marie-Christine; Coll, Jean-Luc

CORPORATE SOURCE: Groupe de Recherche sur le Cancer du Poumon, INSERM U578, Institute Albert Bonniot, La Tronche, 38706, Fr.

SOURCE: Journal of Gene Medicine (2005), 7(7), 936-944

CODEN: JGMEFG; ISSN: 1099-498X

PUBLISHER: John Wiley & Sons Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The herpes simplex virus type 1 (HSV-1) VP22 protein has the property to mediate intercellular trafficking of heterologous proteins fused to its C- or N-terminus. The authors have previously shown improved delivery and enhanced therapeutic effect in vitro and in vivo with a P27-VP22 fusion protein. The authors were interested in studying the spread and biol. activity of VP22 fused to the P53 tumor suppressor. Expression of the VP22-P53 and P53-VP22 fusion proteins was shown by Western blot and intercellular spreading was monitored by immunofluorescence on transiently transfected cells. In vitro antiproliferative activity of wild-type (wt) P53 and P53-VP22 was assessed by proliferation assays and transactivating ability was studied by a reporter gene test and a gel-shift assay. Antitumor activity was also tested in vivo by intratumoral injections of naked DNA in a model of s.c. tumors implanted in nude mice. The authors' results show that the C-terminal fusion or the N-terminal P53-VP22 fusion proteins are not able to spread as efficiently as VP22. Moreover, the authors demonstrate that VP22-P53 does not possess any transactivating ability. P53-VP22 has an antiproliferative activity, but this activity is not superior to the one of P53 alone, in vitro or in vivo. Thus, the authors' study indicates that a gene transfer strategy using VP22 cannot be considered as a universal system to improve the delivery of any protein.

CC 63-5 (Pharmaceuticals)

Section cross-reference(s): 3

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L46 ANSWER 8 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:418599 HCAPLUS

DOCUMENT NUMBER: 142:479681

TITLE: Cooperation of amphiregulin and insulin-like growth factor-1 inhibits Bax- and Bad-mediated apoptosis via a protein kinase C-dependent pathway in non-small cell lung cancer cells

AUTHOR(S): Hurbin, Amandine; Coll, Jean-Luc; Dubrez-Daloz, Laurence; Mari, Bernard; Auberger, Patrick; Brambilla, Christian; Favrot, Marie-Christine

CORPORATE SOURCE: Groupe de Recherche sur le Cancer du Poumon, Institut Albert Bonniot, INSERM U578, La Tronche, 38706, Fr.

SOURCE: Journal of Biological Chemistry (2005), 280(20), 19757-19767

CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Amphiregulin (AR) and insulin-like growth factor-1 (IGF1) are growth factors known to promote non-small cell lung cancer (NSCLC) survival. We have previously published that (1) AR and IGF1, secreted by H358 NSCLC cells, cooperate to protect those cells and H322 NSCLC cells from serum-starved apoptosis; (2) H358 cells resist Bax-induced apoptosis through an inhibition of Bax conformational change. We show here that the antiapoptotic activity of the AR/IGF1 combination is specifically abolished by the PKC inhibitors calphostin C and staurosporine, but not by the MAPK and phosphatidylinositol 3-kinase inhibitors PD98059 and wortmannin, suggesting the involvement of a PKC-dependent and MAPK- and phosphatidylinositol 3-kinase-independent survival pathway. The PKC δ inhibitor rottlerin restores apoptosis induced by serum deprivation. In addition, phosphorylation of PKC δ and PKC ζ/λ , but not of PKC α/β II, increases in serum-starved H358 cells and in H322 cells treated with an AR/IGF1 combination and is blocked by calphostin C. The combination of AR and IGF1 increases p90rsk and Bad phosphorylation as well as inhibiting the conformational change of Bax by a PKC-dependent mechanism. Finally, PKC δ , PKC ζ , or p90rsk small interfering RNAs block the antiapoptotic activity of AR/IGF1 combination but have no effect on partial apoptosis inhibition observed with each factor used alone. Constitutively active PKC expression inhibits serum deprivation-induced apoptosis, whereas a catalytically inactive form of p90rsk restores it. Thus, AR and IGF1 cooperate to prevent apoptosis by activating a specific PKC-p90rsk-dependent pathway, which leads to Bad and Bax inactivation. This signaling pathway is different to that used by single factor.

CC 14-1 (Mammalian Pathological Biochemistry)

Section cross-reference(s): 2

REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L46 ANSWER 9 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:293513 HCAPLUS

DOCUMENT NUMBER: 141:7426

TITLE: Template Assembled Cyclopeptides as Multimeric System

for **Integrin** Targeting and Endocytosis

AUTHOR(S): **Boturyn, Didier; Coll, Jean-Luc; Garanger, Elisabeth; Favrot, Marie-Christine; Dumy, Pascal**

CORPORATE SOURCE: LEDSS, UMR CNRS, Grenoble, 38041, Fr.

SOURCE: Journal of the American Chemical Society (2004), *May 2004*
126(18), 5730-5739
CODEN: JACSAT; ISSN: 0002-7863

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 141:7426

AB The $\alpha\text{V}\beta 3$ **integrin** receptor plays an important role in human metastasis and tumor-induced angiogenesis. Cyclic peptide, cyclo[RGDfV] (f = D-Phe), represents a selective $\alpha\text{V}\beta 3$ **integrin** ligand that has been extensively used for research, therapy, and diagnosis of neoangiogenesis. Here, the authors report the modular synthesis and biol. characterization of template assembled cyclopeptides as a multimeric system for targeting and endocytosis of cells expressing $\alpha\text{V}\beta 3$ **integrin**. Cyclo[RGDfK] was cleanly assembled in a multivalent mode by chemoselective **oxime** bond formation to a cyclodecapeptides template labeled by different reporter groups. Binding propensity to the $\alpha\text{V}\beta 3$ receptor and the associated good uptake property displayed by the multivalent mols. demonstrated the interest in the RAFT mol. to design new multimeric system with hitherto unreported properties. These peptides offer an interesting perspective for the reevaluation of **integrins** as angiogenesis regulators (R. Hynes et al., Nature Med. 2003, 9, 918-921) as well as for the design of more sophisticated systems such as mol. conjugate vectors.

CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 15

ST cyclic multimeric peptide prepn **integrin** receptor binding
endocytosis; RGD peptide fluorescein labeled template assembled synthesis
cyclization

IT Peptides, preparation
RGD peptides
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation);
BIOL (Biological study); PREP (Preparation)
(cyclic; preparation and biol. activity of template-assembled RGD cyclopeptides as multimeric system for **integrin** targeting and endocytosis of cells expressing $\alpha\text{V}\beta 3$ **integrin**)

IT Solid phase synthesis
(peptide; preparation and biol. activity of template-assembled RGD cyclopeptides as multimeric system for **integrin** targeting and endocytosis of cells expressing $\alpha\text{V}\beta 3$ **integrin**)

IT **Integrins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
($\alpha\text{V}\beta 3$; preparation and biol. activity of template-assembled RGD cyclopeptides as multimeric system for **integrin** targeting and endocytosis of cells expressing $\alpha\text{V}\beta 3$ **integrin**)

IT 137813-35-5
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation and biol. activity of template-assembled RGD cyclopeptides as multimeric system for **integrin** targeting and endocytosis of cells expressing $\alpha\text{V}\beta 3$ **integrin**)

IT 188982-03-8P 343312-29-8P 343312-30-1P
343312-31-2P 343312-32-3P 696660-87-4P
697288-12-3P 697288-13-4P 697288-14-5P 697288-15-6P
697288-37-2P 697288-38-3P 697288-39-4P
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation);

BIOL (Biological study); PREP (Preparation)

(preparation and biol. activity of template-assembled RGD cyclopeptides as multimeric system for **integrin** targeting and endocytosis of cells expressing $\alpha\text{V}\beta 3$ **integrin**)

IT 58-85-5, Biotin 108-30-5, Succinic anhydride, reactions 3326-32-7,
FITC (isomer I) 47375-34-8 80366-85-4 280578-04-3
388633-54-3

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation and biol. activity of template-assembled RGD cyclopeptides as multimeric system for **integrin** targeting and endocytosis of cells expressing $\alpha\text{V}\beta 3$ **integrin**)

IT 163395-17-3P 206113-71-5P 343312-28-7P 343312-33-4P
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696660-57-8P 696660-60-3P 696660-63-6P 696660-66-9P 696660-69-2P
696660-70-5P 696660-71-6P 696660-73-8P 696660-75-0P 696660-77-2P
696660-79-4P 696660-81-8P 696660-82-9P 696660-83-0P
696660-84-1P 696660-85-2P 696660-86-3P 696660-88-5P
696660-89-6P 696660-90-9P 696660-91-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and biol. activity of template-assembled RGD cyclopeptides as multimeric system for **integrin** targeting and endocytosis of cells expressing $\alpha\text{V}\beta 3$ **integrin**)

IT 188982-03-8P 343312-29-8P 343312-30-1P
343312-31-2P 343312-32-3P 696660-87-4P
697288-12-3P 697288-14-5P 697288-37-2P
697288-39-4P

RL: BSU (Biological study, unclassified); SPN (Synthetic preparation);

BIOL (Biological study); PREP (Preparation)

(preparation and biol. activity of template-assembled RGD cyclopeptides as multimeric system for **integrin** targeting and endocytosis of cells expressing $\alpha\text{V}\beta 3$ **integrin**)

IT 388633-54-3

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation and biol. activity of template-assembled RGD cyclopeptides as multimeric system for **integrin** targeting and endocytosis of cells expressing $\alpha\text{V}\beta 3$ **integrin**)

IT 343312-28-7P 343312-33-4P 696660-84-1P
696660-88-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and biol. activity of template-assembled RGD cyclopeptides as multimeric system for **integrin** targeting and endocytosis of cells expressing $\alpha\text{V}\beta 3$ **integrin**)

IT 188982-03-8P 343312-29-8P 343312-30-1P
343312-31-2P 343312-32-3P 696660-87-4P
697288-12-3P 697288-14-5P 697288-37-2P
697288-39-4P

RL: BSU (Biological study, unclassified); SPN (Synthetic preparation);

BIOL (Biological study); PREP (Preparation)

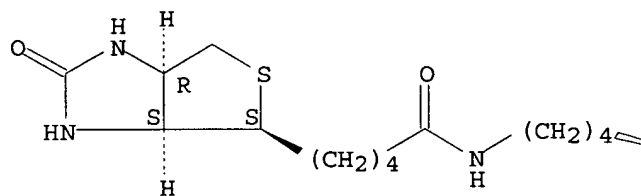
(preparation and biol. activity of template-assembled RGD cyclopeptides as multimeric system for **integrin** targeting and endocytosis of cells expressing $\alpha\text{V}\beta 3$ **integrin**)

RN 188982-03-8 HCAPLUS

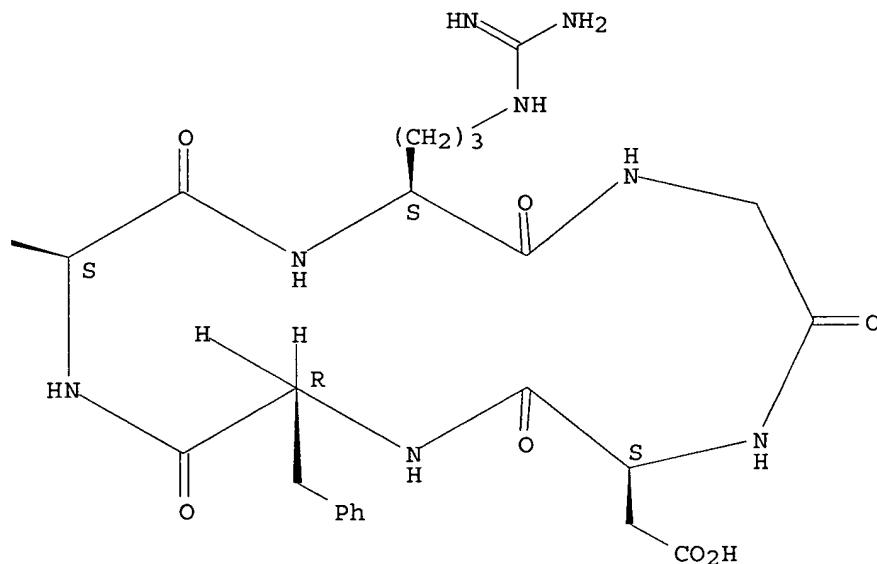
CN Cyclo[L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-N6-[5-
[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-1-oxopentyl]-
L-lysyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

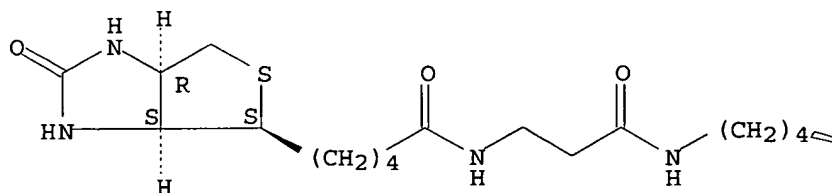


RN 343312-29-8 HCAPLUS

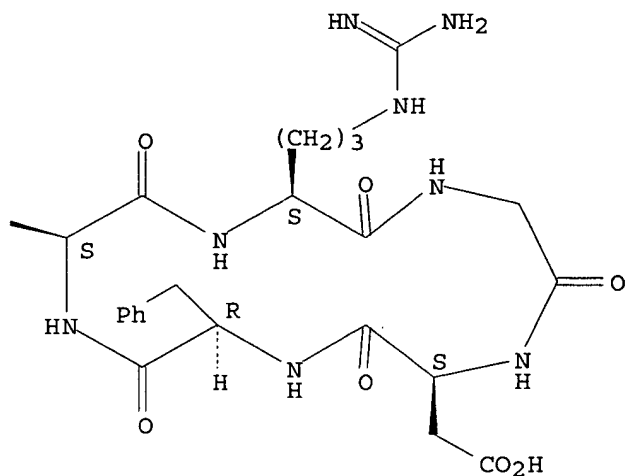
CN Cyclo[L-arginylglycyl-L-α-aspartyl-D-phenylalanyl-N6-[N-[5-
[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-1-oxopentyl]-
β-alanyl]-L-lysyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

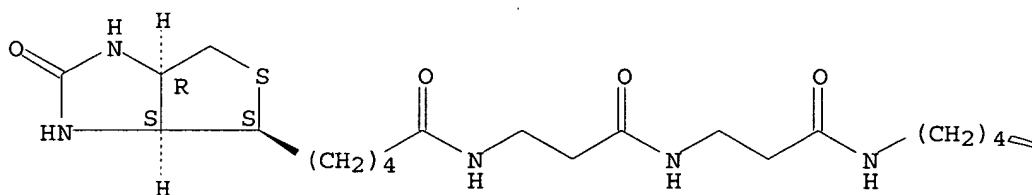


RN 343312-30-1 HCAPLUS

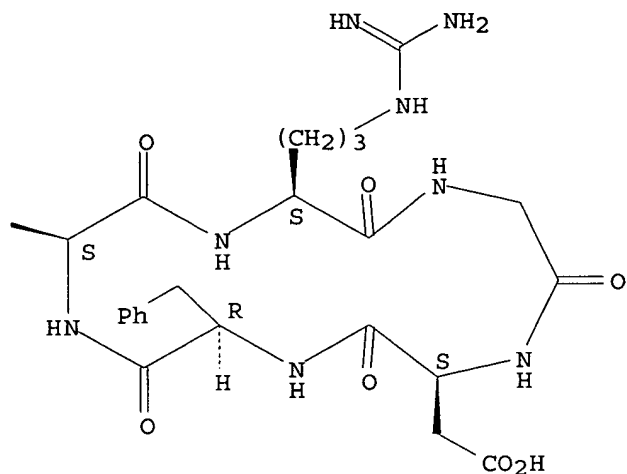
CN Cyclo[L-arginylglycyl-L-α-aspartyl-D-phenylalanyl-N6-[N-[5-
[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-1-oxopentyl]-
β-alanyl-β-alanyl]-L-lysyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

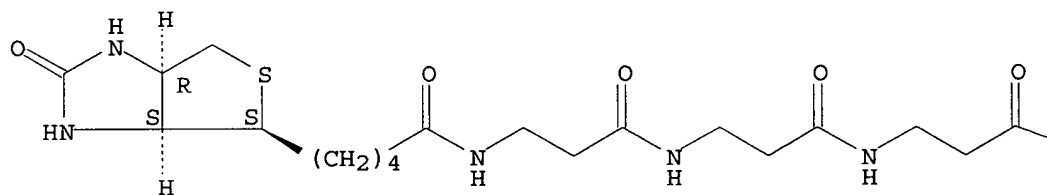


RN 343312-31-2 HCAPLUS

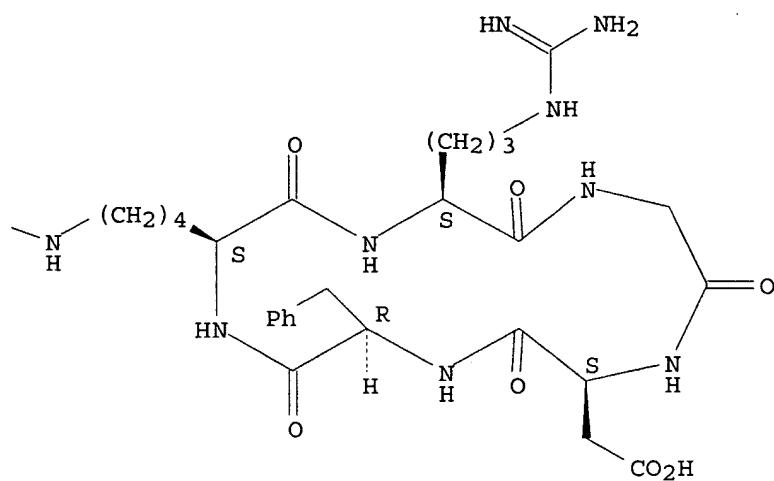
CN Cyclo[L-arginylglycyl-L-α-aspartyl-D-phenylalanyl-N6-[N-[5-
[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-1-oxopentyl]-
β-alanyl-β-alanyl-β-alanyl]-L-lysyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

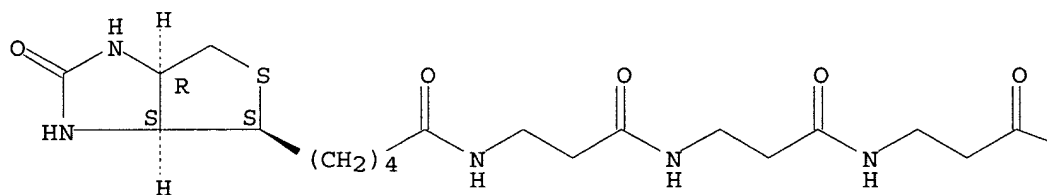


RN 343312-32-3 HCAPLUS

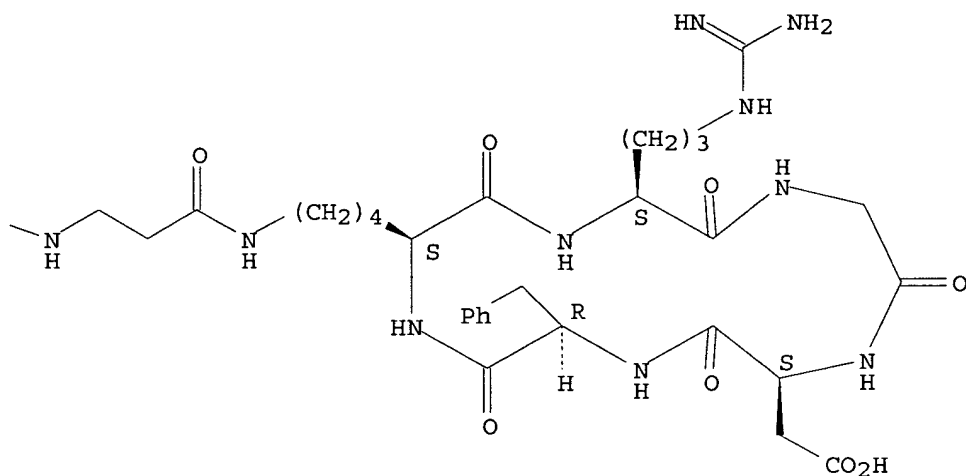
CN Cyclo[L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-N6-[N-[5-
[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-1-oxopentyl]-
 β -alanyl- β -alanyl- β -alanyl- β -alanyl]-L-lysyl] (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

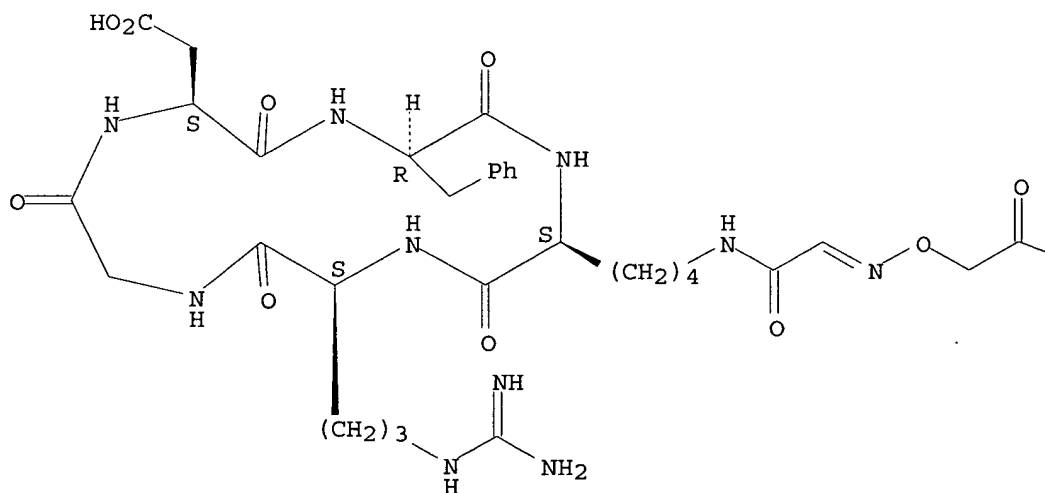


RN 696660-87-4 HCAPLUS

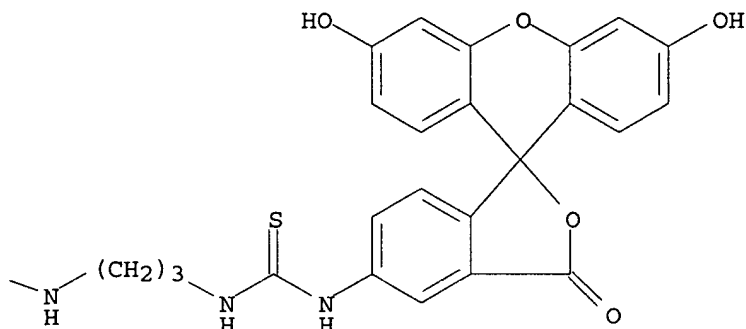
CN Cyclo[L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-N6-[12-[(3',6'-dihydroxy-3-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen]-5-yl)amino]-1,6-dioxo-12-thioxo-4-oxa-3,7,11-triazadodec-2-en-1-yl]-L-lysyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

PAGE 1-A



PAGE 1-B



RN 697288-12-3 HCAPLUS

CN Cyclo[glycyl-N6-[(aminooxy)acetyl]-L-lysyl-N6-[5-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-1-oxopentyl]-L-lysyl-N6-[(aminooxy)acetyl]-L-lysyl-L-prolylglycyl-N6-[(aminooxy)acetyl]-L-lysyl-N6-[5-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-1-oxopentyl]-L-lysyl-N6-[(aminooxy)acetyl]-L-lysyl-L-prolyl], (5'→2), (5'→4), (5'→7), (5'→9) - tetraaldoxime with cyclo[L-arginylglycyl-L-α-aspartyl-D-phenylalanyl-N6-(oxoacetyl)-L-lysyl] (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 697288-14-5 HCAPLUS

CN Cyclo[glycyl-N6-[(aminooxy)acetyl]-L-lysyl-N6-[[3',6'-dihydroxy-3-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen]-5-yl)amino]thioxomethyl]-L-lysyl-N6-[(aminooxy)acetyl]-L-lysyl-L-prolylglycyl-N6-[(aminooxy)acetyl]-L-lysyl-N6-[[3',6'-dihydroxy-3-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen]-5-yl)amino]thioxomethyl]-L-lysyl-N6-[(aminooxy)acetyl]-L-lysyl-L-prolyl], (5'→2), (5'→4), (5'→7), (5'→9) - tetraaldoxime with cyclo[L-arginylglycyl-L-α-aspartyl-D-phenylalanyl-N6-(oxoacetyl)-L-lysyl] (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 697288-37-2 HCAPLUS

CN Cyclo[L-alanyl-N6-[(aminooxy)acetyl]-L-lysyl-L-prolylglycyl-N6-[(aminooxy)acetyl]-L-lysyl-N6-[[3',6'-dihydroxy-3-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen]-5-yl)amino]thioxomethyl]-L-lysyl-N6-[(aminooxy)acetyl]-L-lysyl-L-prolylglycyl-N6-[(aminooxy)acetyl]-L-lysyl], (5'→2), (5'→5), (5'→7), (5'→10) - tetraaldoxime with cyclo[L-arginylglycyl-L-α-aspartyl-D-phenylalanyl-N6-(oxoacetyl)-L-lysyl] (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 697288-39-4 HCAPLUS

CN Cyclo[L-alanyl-N6-[(aminooxy)acetyl]-L-lysyl-L-prolylglycyl-N6-[(aminooxy)acetyl]-L-lysyl-N6-L-tyrosyl-L-lysyl-N6-[(aminooxy)acetyl]-L-lysyl-L-prolylglycyl-N6-[(aminooxy)acetyl]-L-lysyl], (5'→2), (5'→5), (5'→7), (5'→10) - tetraaldoxime with cyclo[L-arginylglycyl-L-α-aspartyl-D-phenylalanyl-N6-(oxoacetyl)-L-lysyl] (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT 388633-54-3

RL: RCT (Reactant); RACT (Reactant or reagent)

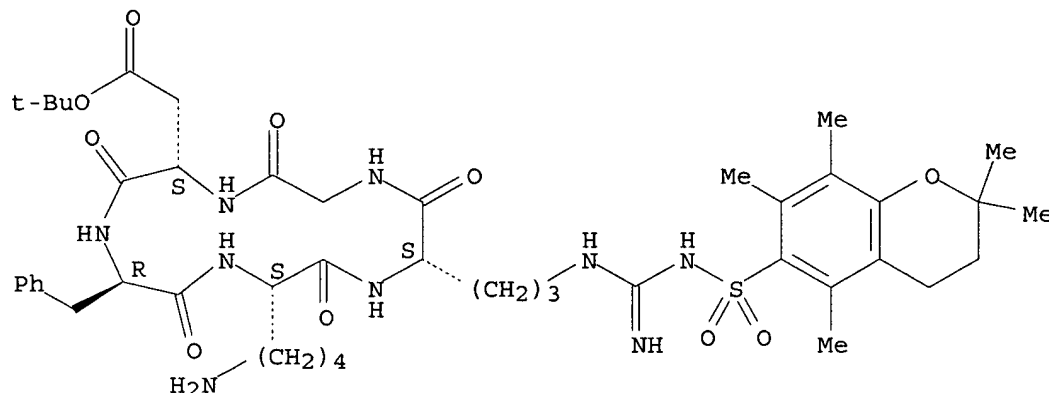
(preparation and biol. activity of template-assembled RGD cyclopeptides as

multimeric system for **integrin** targeting and endocytosis of cells expressing $\alpha V\beta 3$ **integrin**)

RN 388633-54-3 HCAPLUS

CN Cyclo[L- α -aspartyl-D-phenylalanyl-L-lysyl-N5-[[[(3,4-dihydro-2,2,5,7,8-pentamethyl-2H-1-benzopyran-6-yl)sulfonyl]amino]iminomethyl]-L-ornithylglycyl], 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 343312-28-7P 343312-33-4P 696660-84-1P
696660-88-5P

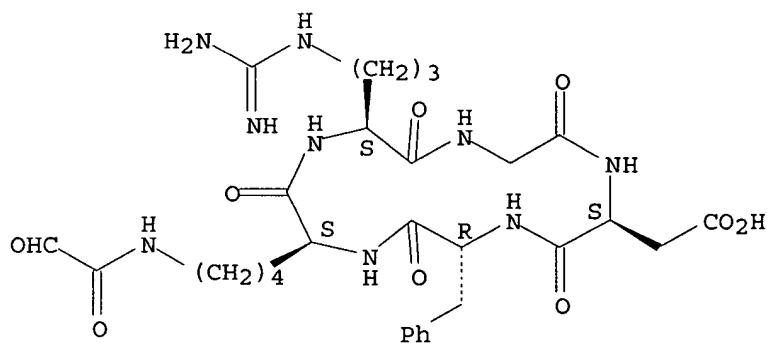
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and biol. activity of template-assembled RGD cyclopeptides as multimeric system for **integrin** targeting and endocytosis of cells expressing $\alpha V\beta 3$ **integrin**)

RN 343312-28-7 HCAPLUS

CN Cyclo[L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-N6-(oxoacetyl)-L-lysyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.

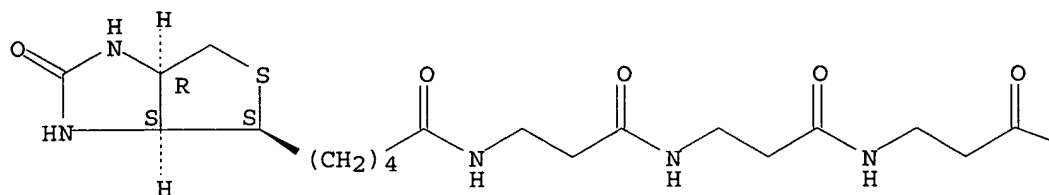


RN 343312-33-4 HCAPLUS

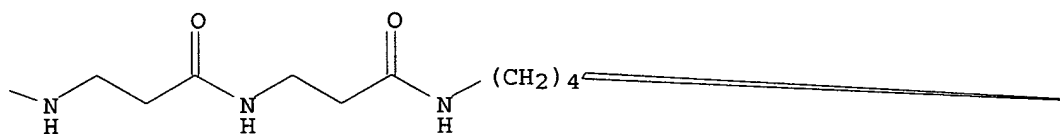
CN Cyclo[L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-N6-[N-[5-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-1-oxopentyl]- β -alanyl- β -alanyl- β -alanyl- β -alanyl- β -alanyl]-L-lysyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.

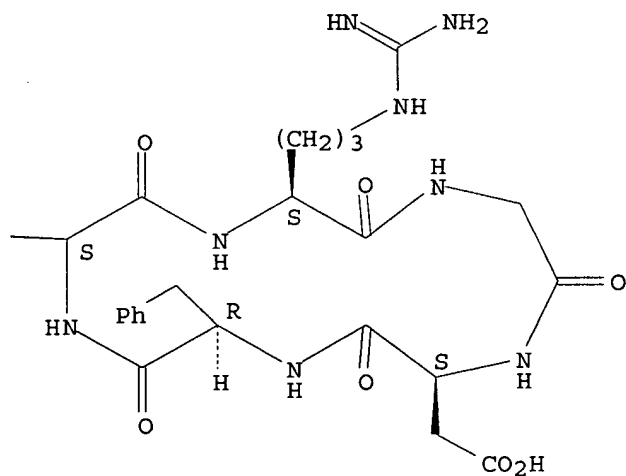
PAGE 1-A



PAGE 1-B



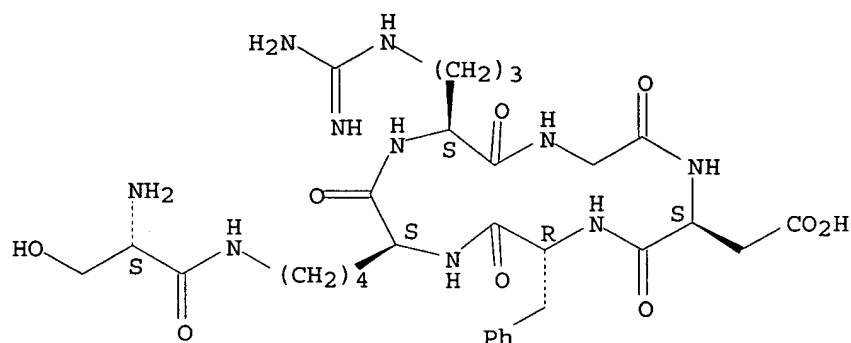
PAGE 1-C



RN 696660-84-1 HCAPLUS

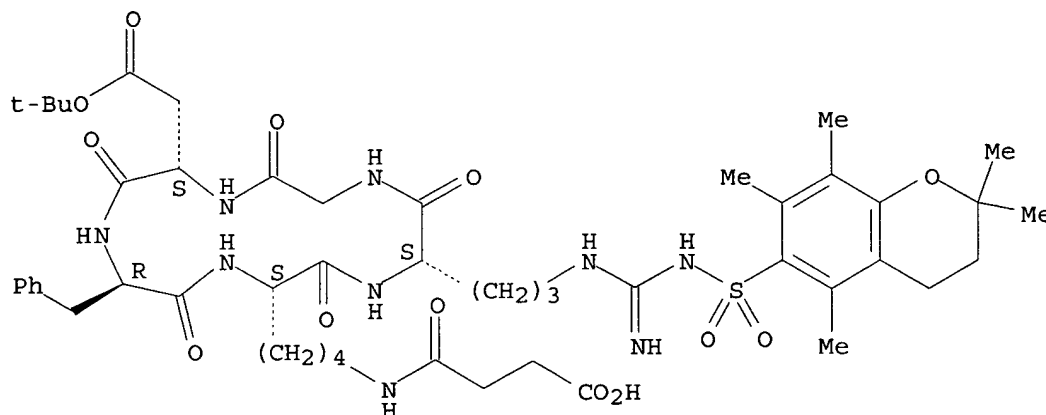
CN Cyclo(L-arginylglycyl-L-α-aspartyl-D-phenylalanyl-N6-L-seryl-L-lysyl) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 696660-88-5 HCAPLUS
 CN Cyclo[L- α -aspartyl-D-phenylalanyl-N6-(3-carboxy-1-oxopropyl)-L-lysyl-N5-[[[(3,4-dihydro-2,2,5,7,8-pentamethyl-2H-1-benzopyran-6-yl)sulfonyl]amino]iminomethyl]-L-ornithylglycyl], 1-(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L46 ANSWER 10 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2004:267350 HCAPLUS
 DOCUMENT NUMBER: 140271202
 TITLE: Synthesis and characterization of novel systems for guidance and vectorization of molecules of therapeutic interest towards target cells
 INVENTOR(S): Dumy, Pascal; Favrot, Marie-Christine; Boturyn, Didier; Coll, Jean-Luc
 PATENT ASSIGNEE(S): Centre National de la Recherche Scientifique - CNRS, Fr.; Universite Joseph Fourier; Institut National de la Sante et de la Recherche Medicale (INSERM)
 SOURCE: PCT Int. Appl., 39 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: French
 FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004026894	A2	20040401	WO 2003-FR2773	20030919
WO 2004026894	A3	20040624		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
FR 2844798	A1	20040326	FR 2002-11614	20020919
FR 2844798	B1	20041112		
CA 2499496	AA	20040401	CA 2003-2499496	20030919
AU 2003299038	A1	20040408	AU 2003-299038	20030919
EP 1539804	A2	20050615	EP 2003-797355	20030919
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2006514919	T2	20060518	JP 2004-537232	20030919
US 2006173160	A1	20060803	US 2005-528320	20051011
PRIORITY APPLN. INFO.:			FR 2002-11614	A 20020919
			US 2002-411845P	P 20020919
			WO 2003-FR2773	W 20030919

AB The invention relates to a method for preparing a **grafted** homodetic cyclopeptide which forms a frame defining two surfaces (upper and lower). The method involves intramol. cyclization of synthesized orthogonally-protected linear peptides, substitution of some or all of the orthogonal protecting groups by a protected precursor, and **grafting** of a mol. of therapeutic interest on one and/or the other surface of the frame by an **oxime** bond. C(RGDfK) is a claimed cyclopentapeptide of interest.

IC ICM C07K001-08

ICS C07K007-64; C07K019-00; A61K038-12; A61P035-00

CC 34-3 (Amino Acids, Peptides, and Proteins)

Section cross-reference(s): 1, 63

IT **Integrins**

RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (synthesis and characterization of novel systems for guidance and
 vectorization of mols. of therapeutic interest towards target cells)

IT **161552-03-0P**

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
 study); PREP (Preparation); USES (Uses)
 (synthesis and characterization of novel systems for guidance and
 vectorization of mols. of therapeutic interest towards target cells)

IT **161552-03-0P**

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
 study); PREP (Preparation); USES (Uses)
 (synthesis and characterization of novel systems for guidance and
 vectorization of mols. of therapeutic interest towards target cells)

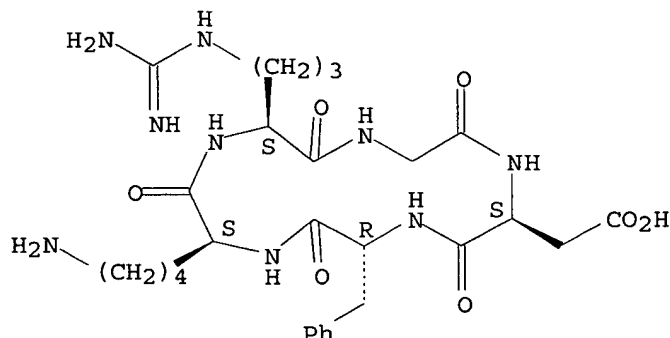
IT **161552-03-0P**

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
 study); PREP (Preparation); USES (Uses)
 (synthesis and characterization of novel systems for guidance and
 vectorization of mols. of therapeutic interest towards target cells)

RN 161552-03-0 HCAPLUS

CN Cyclo(L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-L-lysyl) (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



L46 ANSWER 11 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:253767 HCAPLUS

DOCUMENT NUMBER: 141:271909

TITLE: Inhibition of apoptosis by amphiregulin via an insulin-like growth factor-1 receptor-dependent pathway in non-small cell lung cancer cell lines
AUTHOR(S): Hurbin, Amandine; Dubrez, Laurence; Coll, Jean-Luc; Favrot, Marie C.

CORPORATE SOURCE: Groupe de Recherche sur le Cancer du Poumon, INSERM-U578, Institut Albert Bonniot, La Tronche, 38706, Fr.

SOURCE: Annals of the New York Academy of Sciences (2003), 1010(Apoptosis), 354-357

CODEN: ANYAA9; ISSN: 0077-8923

PUBLISHER: New York Academy of Sciences

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The reciprocal activation of amphiregulin (AR) and insulin-like growth factor-1 (IGF1) pathways has been shown to induce inhibition of serum deprivation apoptosis in non-small cell lung cancer (NSCLC) cell lines H358 and H322. We demonstrated that AR activated the IGF1 receptor (IGF1-R), which in turn induced the secretion of AR and IGF1. Transactivation of the IGF1-R by AR is independent of its binding to EGFR. Thus, AR can inhibit apoptosis in NSCLC cells through an IGF1-R-dependent pathway.

CC 2-10 (Mammalian Hormones)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L46 ANSWER 12 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:249308 HCAPLUS

DOCUMENT NUMBER: 140:271199

TITLE: Synthesis and characterization of novel systems for guidance and vectorization of molecules of therapeutic interest towards target cells

INVENTOR(S): Dumy, Pascal; Favrot, Marie Christine; Boturyn, Didier; Coll, Jean Luc

PATENT ASSIGNEE(S): Centre National de la Recherche Scientifique CNRS, Fr.
SOURCE: Fr. Demande, 26 pp.

DOCUMENT TYPE: Patent
 LANGUAGE: French
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

CODEN: FRXXBL

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2844798	A1	20040326	FR 2002-11614	20020919
FR 2844798	B1	20041112		
CA 2499496	AA	20040401	CA 2003-2499496	20030919
WO 2004026894	A2	20040401	WO 2003-FR2773	20030919
WO 2004026894	A3	20040624		
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003299038	A1	20040408	AU 2003-299038	20030919
EP 1539804	A2	20050615	EP 2003-797355	20030919
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2006514919	T2	20060518	JP 2004-537232	20030919
US 2006173160	A1	20060803	US 2005-528320	20051011
PRIORITY APPLN. INFO.:				
			FR 2002-11614	A 20020919
			US 2002-411845P	P 20020919
			WO 2003-FR2773	W 20030919

AB The invention relates to a method for preparing a **grafted** homodetic cyclopeptide which forms a frame defining two surfaces (upper and lower). The method involves intramol. cyclization of synthesized orthogonally-protected linear peptides, substitution of some or all of the orthogonal protecting groups by a protected precursor, and **grafting** of a mol. of therapeutic interest on one and/or the other surface of the frame by an **oxime** bond. Cyclo(RGDfK) is a claimed cyclopeptide of interest.

IC ICM C07K001-08
 ICS C07K007-64; C07K019-00; A61K038-12; A61P035-00

CC 34-3 (Amino Acids, Peptides, and Proteins)
 Section cross-reference(s): 1, 63

IT **Integrins**
 RL: BSU (Biological study, unclassified); BIOL (Biological study) (synthesis and characterization of novel systems for guidance and vectorization of mols. of therapeutic interest towards target cells)

IT **161552-03-0P**
 RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (synthesis and characterization of novel systems for guidance and vectorization of mols. of therapeutic interest towards target cells)

IT **161552-03-0P**
 RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (synthesis and characterization of novel systems for guidance and vectorization of mols. of therapeutic interest towards target cells)

IT **161552-03-0P**
 RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (synthesis and characterization of novel systems for guidance and vectorization of mols. of therapeutic interest towards target cells)

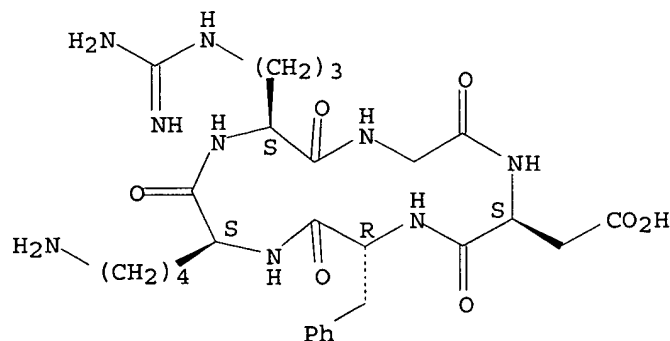
study); PREP (Preparation); USES (Uses)

(synthesis and characterization of novel systems for guidance and vectorization of mols. of therapeutic interest towards target cells)

RN 161552-03-0 HCAPLUS

CN Cyclo(L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-L-lysyl) (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L46 ANSWER 13 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:248674 HCAPLUS

DOCUMENT NUMBER: 141:101771

TITLE: Novel model peptide for Atx1-like metallochaperones

AUTHOR(S): Seneque, Olivier; Crouzy, Serge; Boturyn, Didier; Dumy, Pascal; Ferrand, Michel; Delangle, Pascale

CORPORATE SOURCE: SCIB, CEA/DSM/DRFMC, CEA-Grenoble, Laboratoire de Reconnaissance Ionique, Grenoble, 38054, Fr.

SOURCE: Chemical Communications (Cambridge, United Kingdom) (2004), (7), 770-771

CODEN: CHCOFS; ISSN: 1359-7345

PUBLISHER: Royal Society of Chemistry

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The novel cyclodecapeptide c(GMTCSGCSR) is able to bind soft metals with a selectivity for Hg²⁺ and Cu⁺ over Pb²⁺, Cd²⁺ and Zn²⁺, and is demonstrated to be an excellent structural model of the binding loop of the copper metallochaperone Atx1 in its apo and mercury loaded forms.

CC 6-3 (General Biochemistry)

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L46 ANSWER 14 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:864309 HCAPLUS

DOCUMENT NUMBER: 140:228637

TITLE: VP22-mediated and light-activated delivery of an anti-c-ras antisense oligonucleotide improves its activity after intratumoral injection in nude mice

AUTHOR(S): Zavaglia, David; Normand, Nadia; Brewis, Neil; O'Hare, Peter; Favrot, Marie-Christine; Coll, Jean-luc

CORPORATE SOURCE: Lung Cancer Research Group, INSERM U578, Albert Bonniot Institute, Grenoble, 38706, Fr.

SOURCE: Molecular Therapy (2003), 8(5), 840-845
CODEN: MTOHCK; ISSN: 1525-0016
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB VP22, a protein of the herpes simplex virus tegument, can form complexes with fluorescein-labeled oligonucleotides. These particles, termed "Vectosomes," are efficiently taken up by cells and remain stable in the cell cytoplasm without any particular activity. Interestingly, these Vectosomes can be disrupted by light, which releases the antisense activity. Here we show that anti-c-rafl Vectosomes are efficiently activated by light in vivo after injection into s.c. A549 (non-small-cell lung cancer) tumors implanted in nude mice. Moreover, two injections per wk of anti-c-rafl Vectosomes followed by illumination result in a stronger inhibition of tumor growth than injections of the antisense alone or of the different control Vectosomes. This effect correlates with a strong inhibition of the c-Rafl protein expression. As a consequence of c-Rafl loss, apoptosis was also detected in these tumors. Vectosomes thus represent a new powerful tool to improve the delivery of oligonucleotides in vitro and in vivo.

CC 1-6 (Pharmacology)

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L46 ANSWER 15 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:714434 HCAPLUS

DOCUMENT NUMBER: 140:218078

TITLE: Highly Efficient Synthesis of Peptide- and Carbohydrate-Oligonucleotide Conjugates Using Chemoselective Oxime and Thiazolidine Formation

AUTHOR(S): Forget, D.; Boturyn, D.; Renaudet, O.; Defrancq, E.; Dumy, P.

CORPORATE SOURCE: LEDSS, Universite Joseph Fourier, Grenoble, F-38041, Fr.

SOURCE: Nucleosides, Nucleotides & Nucleic Acids (2003), 22(5-8), 1427-1429

CODEN: NNNAFY; ISSN: 1525-7770

PUBLISHER: Marcel Dekker, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A symposium report. The conjugation of a peptide to the 5'- or the 3'-end of an oligonucleotide was achieved by reaction of an aldehyde moiety with an aminooxy or a 1,2-aminothiol to form an oxime ether or a thiazolidine, resp. The conjugation of carbohydrates was performed via oxime bond formation using aminooxy sugar derivs.

CC 34-3 (Amino Acids, Peptides, and Proteins)

Section cross-reference(s): 33

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L46 ANSWER 16 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:131131 HCAPLUS

DOCUMENT NUMBER: 139:122555

TITLE: Intercellular trafficking and enhanced in vivo antitumour activity of a non-virally delivered P27-VP22 fusion protein

AUTHOR(S): Zavaglia, D.; Favrot, M-C.; Eymin, B.; Tenaud, C.; Coll, J-L.

CORPORATE SOURCE: Groupe Rech. Cancer Poumon, Equipe INSERM 9924, Inst. Albert Bonniot, Fr.

SOURCE: Gene Therapy (2003), 10(4), 314-325
CODEN: GETHEC; ISSN: 0969-7128
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English

AB VP22, a structural protein from herpes simplex virus type I, exhibits the unique property of intercellular trafficking. This protein is exported from primary expressing cells and subsequently imported into neighboring cells. This property is conserved when VP22 is genetically fused to a protein, making it a promising tool to enhance the delivery of a gene product. We chose to study the intercellular transport and biol. effect of a fusion protein between the putative tumor suppressor gene p27Kip1 and VP22. We show that in vitro, P27VP22 is able to spread as efficiently as VP22. Functionality of the P27VP22 protein was demonstrated by its ability to inhibit cyclin/CDK2 complexes activity. In proliferation and clonogenicity assays, transfection with the P27VP22 plasmid resulted in a stronger cell growth inhibition when compared to transfection with the p27Kip1 vector. In vivo, s.c. tumors established in nude mice were injected with naked DNA encoding P27 or P27VP22. Our results show that P27VP22 can spread in vivo and that injections of the P27VP22 plasmid resulted in a significantly greater antitumor activity than injections of the P27 plasmid. This study confirms the usefulness of VP22-mediated delivery and suggests that P27VP22 may have applications in cancer gene therapy.

CC 63-5 (Pharmaceuticals)

Section cross-reference(s): 1, 3

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L46 ANSWER 17 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:108850 HCAPLUS

DOCUMENT NUMBER: 138:283484

TITLE: Non invasive optical imaging of firefly luciferase gene expression in mice using the Berthold Technologies Night OWL LB 981

AUTHOR(S): Coll, J. L.; Favrot, M. C.; Hennecke, M.

CORPORATE SOURCE: INSERM EMI 9924, La Tronche, 38706, Fr.

SOURCE: Bioluminescence & Chemiluminescence: Progress & Current Applications, [Proceedings of the Symposium on Bioluminescence and Chemiluminescence], 12th, Cambridge, United Kingdom, Apr. 5-9, 2002 (2002), 497-500. Editor(s): Stanley, Philip E.; Kricka, Larry J. World Scientific Publishing Co. Pte. Ltd.: Singapore, Singapore.
CODEN: 69DPGZ; ISBN: 981-238-156-2

DOCUMENT TYPE: Conference

LANGUAGE: English

AB Bioluminescent imaging was used to evaluate the growth and metastasis of luciferase transfected tumors in nude mice. Light source measurement are precise and reproducible since the NightOWL LB 981 is calibrated with a light emitting diode (LED). Noninvasive bioluminescent imaging combines the advantages of standardization and quantification known from the in vitro assays with special resolution and the possibility to do long term observation of alive mice.

CC 9-4 (Biochemical Methods)

Section cross-reference(s): 3, 73

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L46 ANSWER 18 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:952675 HCAPLUS

DOCUMENT NUMBER: 138:232126

TITLE: Inhibition of Apoptosis by Amphiregulin via an Insulin-like Growth Factor-1 Receptor-dependent Pathway in Non-small Cell Lung Cancer Cell Lines

AUTHOR(S): Hurbin, Amandine; Dubrez, Laurence; Coll, Jean-Luc; Favrot, Marie-Christine

CORPORATE SOURCE: INSERM-EMI 9924, Groupe de Recherche sur le Cancer du Poumon, Institut Albert Bonniot, La Tronche, 38706, Fr.

SOURCE: Journal of Biological Chemistry (2002), 277(51), 49127-49133

CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Several abnormalities in the insulin-like growth factor-1 (IGF1) and erbB receptors pathways stimulate the growth and survival of lung cancer cells, but their mechanisms of action and cooperation are poorly understood. In this report, we have identified a new mechanism of apoptosis inhibition by amphiregulin through an IGF1-dependent survival pathway in non-small cell lung cancer (NSCLC) cells: amphiregulin activates the IGF1 receptor that in turn induces the secretion of amphiregulin and IGF1. In the absence of serum, the NSCLC cell line H358 resists apoptosis and secretes factors protecting the NSCLC cell line H322 from serum deprivation apoptosis. IGF1 receptor inhibitor AG 1024 as well as epidermal growth factor receptor inhibitors AG 556 and ZD 1839 restore apoptosis in H322 cells cultured in H358-conditioned medium. Accordingly, the anti-apoptotic activity of H358-conditioned medium is completely abolished after incubation with anti-amphiregulin neutralizing antibody and only partially with anti-IGF1 neutralizing antibody. H358-conditioned medium and amphiregulin induce IGF1 receptor phosphorylation in H322 cells, which is prevented by anti-amphiregulin neutralizing antibody but not by AG 556 or ZD 1839. H358 cells secrete a high level of amphiregulin that, in combination with IGF1, prevents serum deprivation apoptosis. Finally, IGF1 receptor inhibitor blocks amphiregulin and IGF1 release by H358 cells.

CC 2-10 (Mammalian Hormones)

REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L46 ANSWER 19 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:905967 HCAPLUS

DOCUMENT NUMBER: 136:193818

TITLE: Cell cycle arrest is sufficient for p53-mediated tumor regression

AUTHOR(S): Dubrez, L.; Coll, J-L.; Hurbin, A.; De Fraipont, F.; Lantejoul, S.; Favrot, M-C.

CORPORATE SOURCE: Groupe de Recherche sur le Cancer du Poumon, Equipe INSERM 9924, Institut Albert Bonniot, La Tronche, 38706, Fr.

SOURCE: Gene Therapy (2001), 8(22), 1705-1712

CODEN: GETHEC; ISSN: 0969-7128

PUBLISHER: Nature Publishing Group

DOCUMENT TYPE: Journal

LANGUAGE: English

AB P53 gene therapy can induce tumor regression, but the low efficacy of in vivo gene transfer has greatly hampered the mechanistic anal. of this

antitumoral activity. The authors therefore used a p53-null human NSCLC cell line in which they reintroduced the wild-type p53 gene under control of a tetracycline-dependent promoter. P53 induction provokes cell cycle arrest in G0/G1 and G2/M phase, an up-regulation of p21, a down-regulation of cyclin B1, and the appearance of senescence features without down-regulation of human telomerase reverse transcriptase. No detectable morphol. changes of apoptosis nor procaspase-3 activation are observed. In s.c. tumors grafted in nude mice, the induction of p53 expression leads to a complete and long-lasting tumor regression in 28 days which is associated with cell cycle arrest, but not detectable apoptosis nor inhibition of angiogenesis. These results show that irreversible cell cycle arrest is sufficient to elicit tumor regression after p53 gene transfer in p53-deficient tumor cells.

CC 1-6 (Pharmacology)

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L46 ANSWER 20 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:905525 HCAPLUS

DOCUMENT NUMBER: 136:263374

TITLE: 3'-Oligonucleotides conjugation via chemoselective oxime bond formation

AUTHOR(S): Forget, Damien; Renaudet, Olivier; **Boturyn, Didier**; Defrancq, Eric; **Dumy, Pascal**

CORPORATE SOURCE: UMR CNRS 5616, LEDSS, Universite Joseph Fourier, Grenoble, F-38041, Fr.

SOURCE: Tetrahedron Letters (2001), 42(52), 9171-9174
CODEN: TELEAY; ISSN: 0040-4039

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 136:263374

AB Chemoselective oxime ligation of cyclo-peptide, fluorescein and mannose derivs. at the 3'-end of an oligonucleotide was achieved. The conjugation was performed by reacting oxy-amine containing reporter groups to an oligonucleotide bearing an aldehyde at the 3'-extremity. The aldehyde was generated by mild periodate oxidation of a 1,2-amino alc. which was readily incorporated at the 3'-end by automated DNA synthesis using the corresponding com. available support. The straight-forward chemical access, their stability in biol. media as well as their unchanged hybridization properties emphasize the interest of such 3'-conjugates.

CC 33-10 (Carbohydrates)

Section cross-reference(s): 34

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L46 ANSWER 21 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:783495 HCAPLUS

DOCUMENT NUMBER: 136:67933

TITLE: Caffeine sensitizes human H358 cell line to p53-mediated apoptosis by inducing mitochondrial translocation and conformational change of BAX protein

AUTHOR(S): Dubrez, Laurence; Coll, **Jean-Luc**; Hurbin, Amandine; Solary, Eric; **Favrot, Marie-Christine**

CORPORATE SOURCE: Groupe de Recherche sur le Cancer du Poumon, INSERM E9924, Institut Albert Bonniot, La Tronche, 38706, Fr.

SOURCE: Journal of Biological Chemistry (2001), 276(42), 38980-38987
CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The mechanisms involved in p53-mediated cell death remain controversial. In the present study, we investigated this cell death pathway by stably transfecting the p53-null H358 cell line with a tetracycline-dependent wild type p53-expressing vector. Restoration of p53 triggered a G2/M cell cycle arrest and enhanced BAX protein expression, without inducing apoptosis or potentiating the cytotoxic effect of etoposide, vincristine, and cisplatinum. Accordingly, overexpression of BAX in H358 cells, through stable transfection of a tetracycline-regulated expression vector, did not induce cell death. Interestingly, the methylxanthine caffeine (4 mM) promoted the translocation of BAX from the cytosol to the mitochondria. In the setting of an overexpression of BAX, caffeine induced a conformational change of the protein and apoptosis. The consequences of caffeine were independent of its cell cycle-related activities. All together, caffeine synergizes with p53 for inducing cell death through a cell cycle-independent mechanism, involving mitochondrial translocation and conformational change of BAX protein.
CC 14-1 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 1, 13
REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L46 ANSWER 22 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:743883 HCAPLUS
DOCUMENT NUMBER: 136:135007
TITLE: Highly efficient synthesis of peptide-oligonucleotide conjugates: chemoselective **oxime** and thiazolidine formation
AUTHOR(S): Forget, Damien; **Boturyn, Didier**; Defrancq, Eric; Lhomme, Jean; **Dumy, Pascal**
CORPORATE SOURCE: LEDSS, UMR CNRS 5616, Universite Joseph Fourier, Grenoble, 38041, Fr.
SOURCE: Chemistry--A European Journal (2001), 7(18), 3976-3984
CODEN: CEUJED; ISSN: 0947-6539
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 136:135007
AB A convergent strategy for the synthesis of peptide-oligonucleotide conjugates (POC) is presented. Chemoselective ligation of peptide to oligonucleotide was accomplished by **oxime** and thiazolidine formation. **Oxime** conjugation was performed by treating an oxyamine-containing peptide with an aldehyde-containing oligonucleotide or vice versa. Ligation by thiazolidine formation was achieved by coupling a peptide, acylated with a cysteine residue, to an oligonucleotide that was derivatized by an aldehyde function. For both approaches, the conjugates were obtained in good yield without the need for a protection strategy and under mild aqueous conditions. Moreover, the **oxime** ligation proved useful for directly conjugating duplex oligonucleotides. Combined with mol. biol. tools, this methodol. opens up new prospects for post-functionalization of high-mol.-weight DNA structures.
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 6, 33
ST peptide oligonucleotide conjugate prepn chemoselective **oxime** thiazolidine formation; oxyamine peptide coupling aldehyde oligonucleotide; cysteine peptide solid phase synthesis aldehyde oligonucleotide; DNA hybridization oligodeoxyribonucleotide duplexes

- IT Nucleic acid hybridization
(DNA-DNA; preparation of peptide-oligonucleotide conjugates via **oxime** and thiazolidine formation by coupling and hybridization properties of oligodeoxyribonucleotide duplexes)
- IT Peptides, preparation
RL: SPN (Synthetic preparation); PREP (Preparation)
(conjugates with oligonucleotides; preparation of peptide-oligonucleotide conjugates via **oxime** and thiazolidine formation by coupling and hybridization properties of oligodeoxyribonucleotide duplexes)
- IT Oligonucleotides
RL: SPN (Synthetic preparation); PREP (Preparation)
(conjugates with peptides; preparation of peptide-oligonucleotide conjugates via **oxime** and thiazolidine formation by coupling and hybridization properties of oligodeoxyribonucleotide duplexes)
- IT Oligodeoxyribonucleotides
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(duplexes; preparation of peptide-oligonucleotide conjugates via **oxime** and thiazolidine formation by coupling and hybridization properties of oligodeoxyribonucleotide duplexes)
- IT Solid phase synthesis
(peptide; preparation of peptide-oligonucleotide conjugates via **oxime** and thiazolidine formation using solid phase peptide synthesis and hybridization properties of oligodeoxyribonucleotide duplexes)
- IT Conjugation (bond)
Peptide coupling
(preparation of peptide-oligonucleotide conjugates via **oxime** and thiazolidine formation by coupling and hybridization properties of oligodeoxyribonucleotide duplexes)
- IT 389095-31-2P 389095-32-3P 389150-83-8P 389150-84-9P 389150-85-0P
393194-56-4P
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(preparation of peptide-oligonucleotide conjugates via **oxime** and thiazolidine formation by coupling and hybridization properties of oligodeoxyribonucleotide duplexes)
- IT 106-69-4, 1,2,6-Hexanetriol 123-11-5, 4-Methoxybenzaldehyde, reactions
4286-55-9 21715-90-2 80366-85-4 89992-70-1 102691-36-1
343312-38-9 388633-60-1D, resin-bound
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of peptide-oligonucleotide conjugates via **oxime** and thiazolidine formation by coupling and hybridization properties of oligodeoxyribonucleotide duplexes)
- IT 52370-39-5P 341016-86-2P **343312-27-6P** **343312-28-7P**
388633-50-9P 388633-51-0P 388633-52-1P 388633-53-2P
388633-54-3P **388633-55-4P** 388633-56-5P 388633-57-6P
388633-58-7P 388633-59-8P 388633-61-2P 388633-62-3P 389095-29-8P
389150-78-1P 389150-79-2P 389150-80-5P 393194-52-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of peptide-oligonucleotide conjugates via **oxime** and thiazolidine formation by coupling and hybridization properties of oligodeoxyribonucleotide duplexes)
- IT **388633-63-4P** **388633-64-5P** 389095-30-1P 389150-77-0P
389150-81-6P 389150-82-7P 393194-53-1P 393194-54-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of peptide-oligonucleotide conjugates via **oxime** and thiazolidine formation by coupling and hybridization properties of oligodeoxyribonucleotide duplexes)
- IT **343312-27-6P** **343312-28-7P** **388633-54-3P**

388633-55-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of peptide-oligonucleotide conjugates via **oxime** and thiazolidine formation by coupling and hybridization properties of oligodeoxyribonucleotide duplexes)

IT **388633-63-4P 388633-64-5P**

RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation of peptide-oligonucleotide conjugates via **oxime** and thiazolidine formation by coupling and hybridization properties of oligodeoxyribonucleotide duplexes)

IT **343312-27-6P 343312-28-7P 388633-54-3P****388633-55-4P**

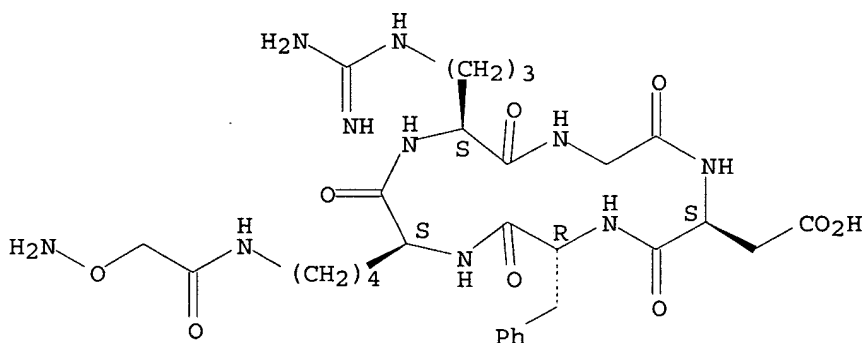
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of peptide-oligonucleotide conjugates via **oxime** and thiazolidine formation by coupling and hybridization properties of oligodeoxyribonucleotide duplexes)

RN 343312-27-6 HCAPLUS

CN Cyclo[L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-N6-[(aminooxy)acetyl]-L-lysyl] (9CI) (CA INDEX NAME)

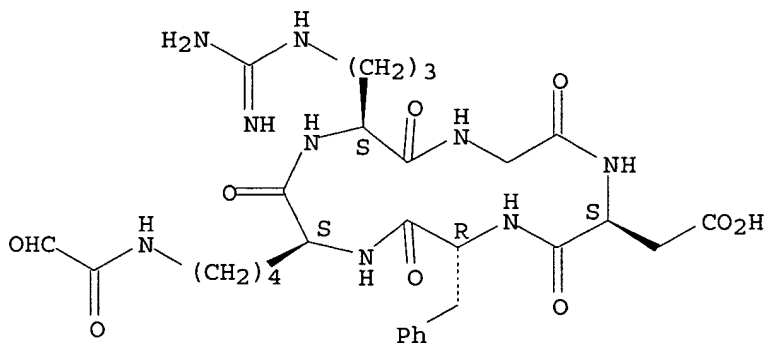
Absolute stereochemistry.



RN 343312-28-7 HCAPLUS

CN Cyclo[L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-N6-(oxoacetyl)-L-lysyl] (9CI) (CA INDEX NAME)

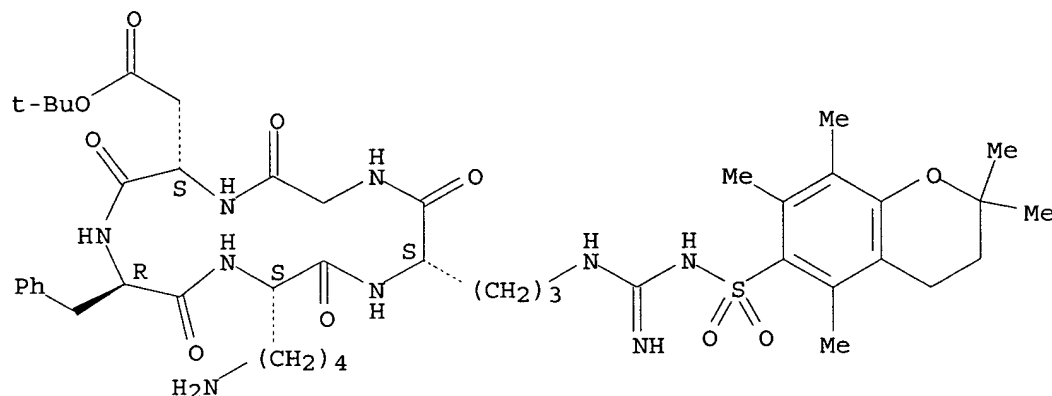
Absolute stereochemistry.



RN 388633-54-3 HCAPLUS

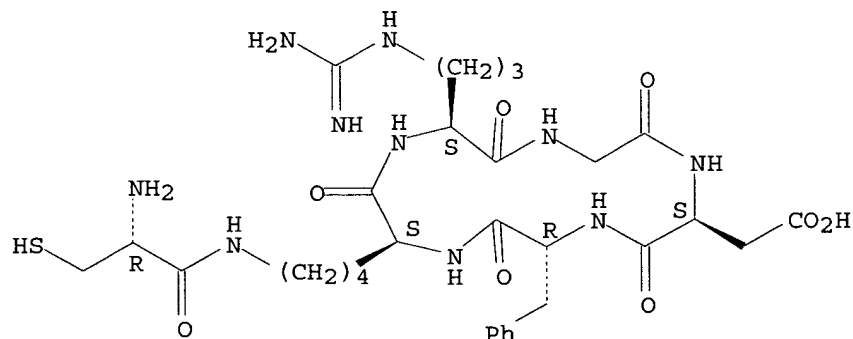
CN Cyclo[L- α -aspartyl-D-phenylalanyl-L-lysyl-N5-[[[(3,4-dihydro-

Absolute stereochemistry.



CN Cyclo(L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-N6-L-cysteinyl-L-lysyl) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RL: SPN (Synthetic preparation); PREP (Preparation)

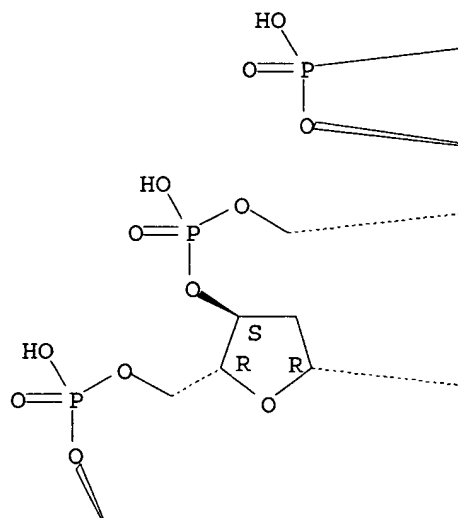
(preparation of peptide-oligonucleotide conjugates via oxime and thiazolidine formation by coupling and hybridization properties of oligodeoxyribonucleotide duplexes)

CN Thymidine, 5'-O-phosphonothymidylyl-(3'→5')-thymidylyl-

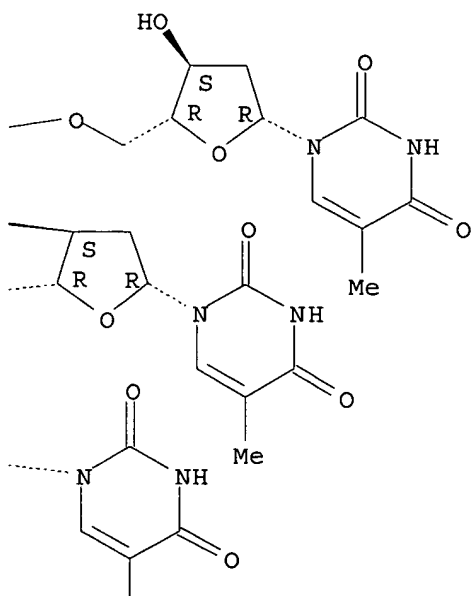
(3'→5')-thymidylyl-(3'→5')-thymidylyl-(3'→5')-
thymidylyl-(3'→5')-thymidylyl-(3'→5')-thymidylyl-
(3'→5')-, (5'→5)-ester with cyclo[L-arginylglycyl-L-α-
aspartyl-D-phenylalanyl-N6-[[(5-hydroxyphenetylidene)amino]oxy]acetyl]-L-
lysyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

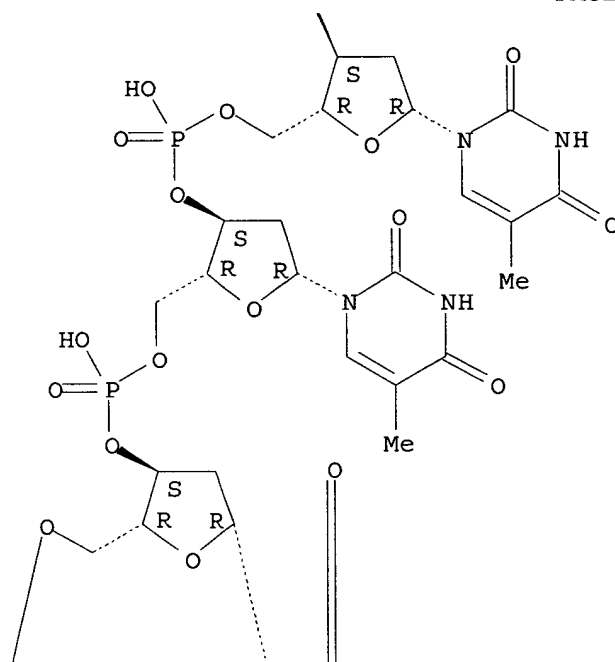
PAGE 1-A



PAGE 1-B



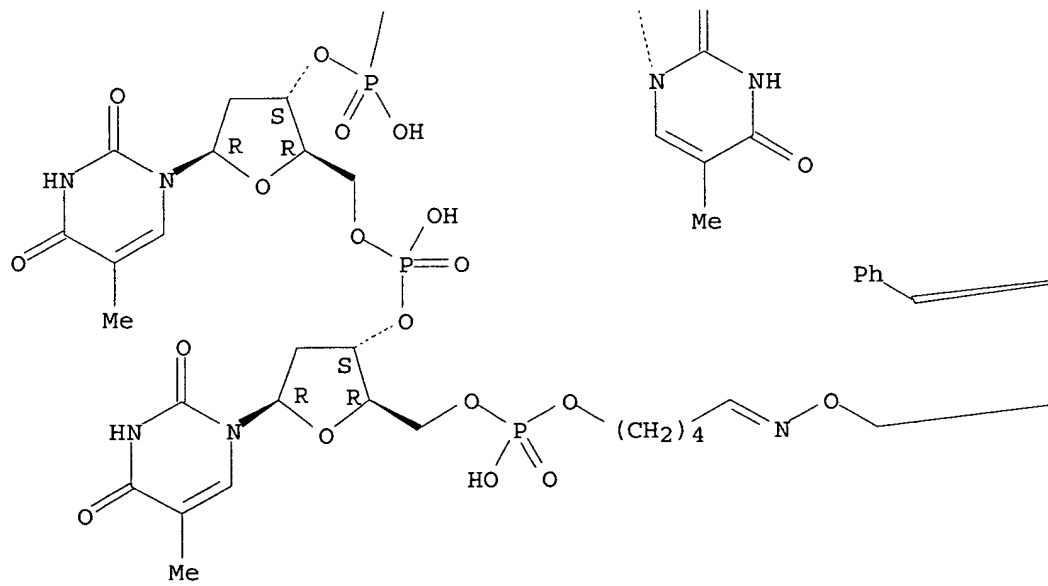
PAGE 2-A



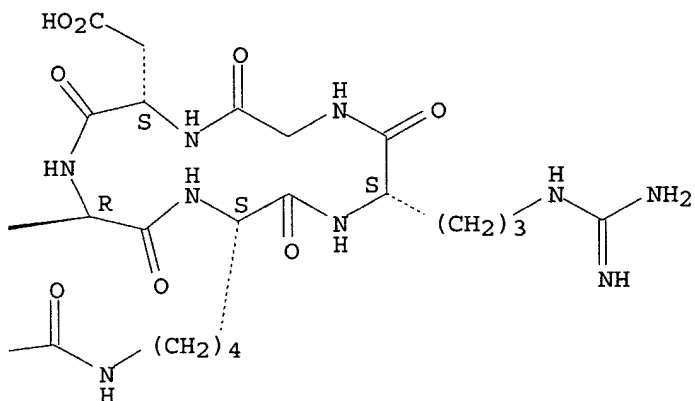
PAGE 2-B

Me

PAGE 3-A



PAGE 3-B

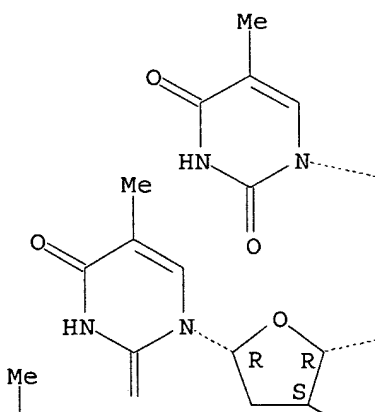


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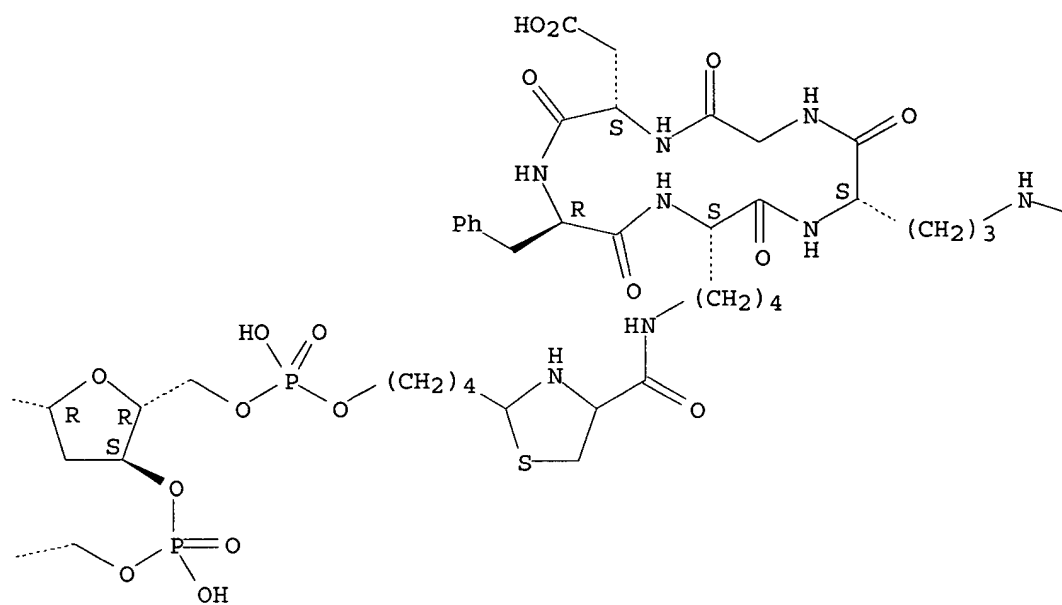
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(3'→5')-thymidylyl-(3'→5')-thymidylyl-(3'→5')-
thymidylyl-(3'→5')-thymidylyl-(3'→5')-thymidylyl-
(3'→5')-, (5'→5)-ester with cyclo[L-arginylglycyl-L-α-
aspartyl-D-phenylalanyl-N6-[[2-(4-hydroxybutyl)-4-thiazolidinyl]carbonyl]-
L-lysyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.

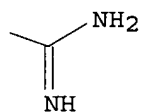
PAGE 1-A



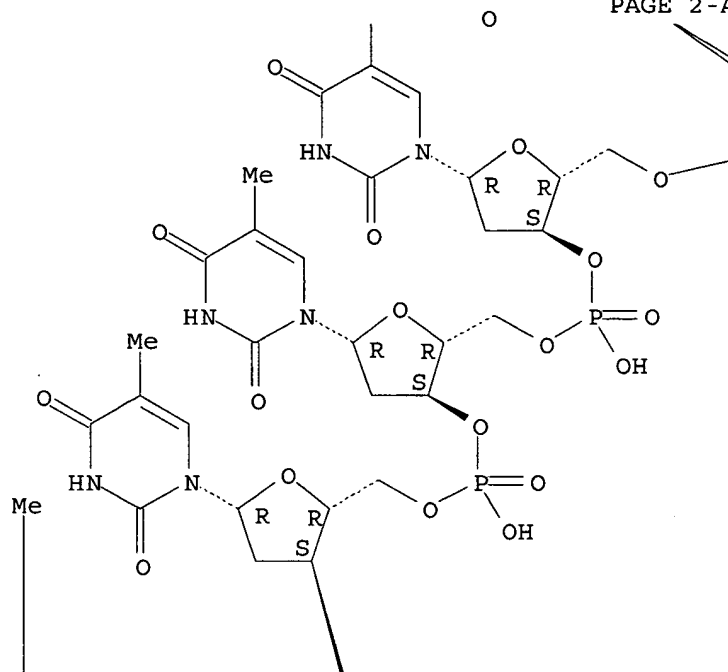
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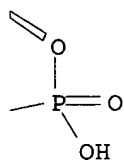
PAGE 1-C



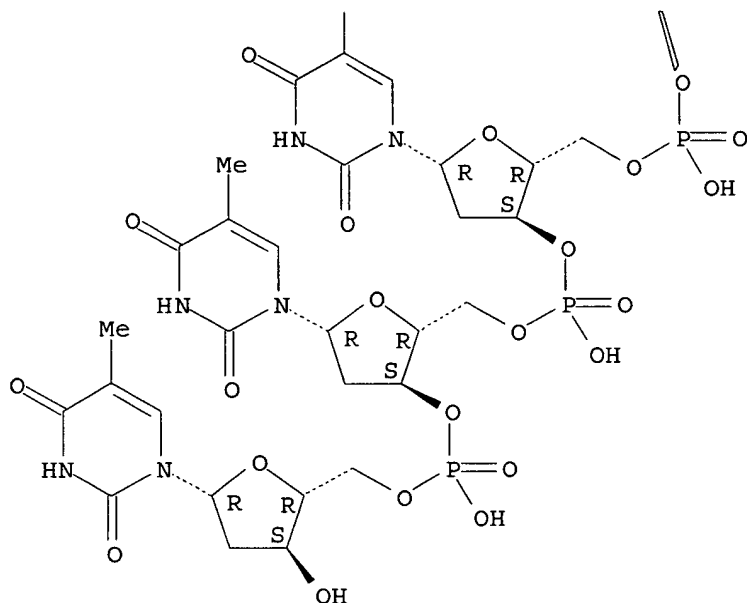
PAGE 2-A



PAGE 2-B



PAGE 3-A



REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L46 ANSWER 23 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:246233 HCAPLUS

DOCUMENT NUMBER: 135:19900

TITLE: A convenient access to α V β 3/ α V β 5 integrin ligand conjugates: regioselective solid-phase functionalisation of an RGD based peptide

AUTHOR(S): Boturyn, Didier; Dumy, Pascal

CORPORATE SOURCE: LEDSS, Ingenierie Molculaire et Chimie des Composes Bioorganiques, BP 53, UMR CNRS 5616, Universite Joseph Fourier, Grenoble, 38041, Fr.

SOURCE: Tetrahedron Letters (2001), 42(15), 2787-2790

CODEN: TELEAY; ISSN: 0040-4039

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The cyclopeptide (-RGDfK-) (f = D-phenylalanine) is a potent and selective α V β 3/ α V β 5 integrin ligand. A methodol. for the conjugation of cyclo(-RGDfK-) through the regioselective derivatization of lysine side chains, either in solution or directly on the solid support, is described. This provides a rapid and flexible chemical entry to conjugated integrin ligands bearing reporter groups for biol. investigations or reactive chemical functions for the preparation of new vector systems.

CC 34-3 (Amino Acids, Peptides, and Proteins)

Section cross-reference(s): 6

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L46 ANSWER 24 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:443042 HCAPLUS

DOCUMENT NUMBER: 131:204515

TITLE: In vivo delivery to tumors of DNA complexed with linear polyethylenimine

AUTHOR(S): Coll, Jean-Luc; Chollet, Patrice; Brambilla, Elisabeth; Desplanques, Dominique; Behr, Jean-Paul; Favrot, Marie
 CORPORATE SOURCE: Lung Cancer Research Group, Institut Albert Bonniot, Universite Joseph Fourier, Grenoble, 38706, Fr.
 SOURCE: Human Gene Therapy (1999), 10(10), 1659-1666
 CODEN: HGTHE3; ISSN: 1043-0342
 PUBLISHER: Mary Ann Liebert, Inc.
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB Synthetic gene delivery vectors have shown promise in several organs, including brain and lung. Tumor cell targeting, however, is still hindered by their low efficacy. A linear polyethylenimine (L-PEI, Exgen 500) was found to be effective in vivo. Our first attempts to use L-PEI for intratumoral gene delivery were not successful, presumably because of poor diffusion of the complexes within the tumor mass after injection with a syringe. Here we show that L-PEI-mediated transfection can be strongly enhanced when the complexes are delivered slowly into a solid tumor mass, using a micropump. Furthermore, L-PEI/DNA complexes actively transfect pseudocystic tumor cells when injected into the cyst cavity. In both cases L-PEI induced a significant and long-lasting (≥ 15 days) expression of the reporter gene. Finally, even though systemic delivery of L-PEI/DNA complexes leads to high levels of expression in the lung, this method is not adapted for transfection of s.c. tumors implanted in the thigh nor for transfection of lung metastases. Altogether, these results show that L-PEI has promising features for transfection of tumor cells, provided that the mode of delivery is adapted.

CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 1

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L46 ANSWER 25 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:788064 HCAPLUS

DOCUMENT NUMBER: 130:191244

TITLE: Gene therapy

AUTHOR(S): Brambilla, Christian; Negoescu, Adrien; Favrot, Marie; Coll, Jean-Luc

CORPORATE SOURCE: Institut Albert Bonniot, Centre Hospitalier Universitaire de Grenoble, Grenoble, Fr.

SOURCE: Lung Biology in Health and Disease (1999), 124(Lung Tumors), 729-745

CODEN: LBHDD7; ISSN: 0362-3181

PUBLISHER: Marcel Dekker, Inc.

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review, with 106 refs., of the use of gene therapy in the treatment of cancer.

CC 1-0 (Pharmacology)

REFERENCE COUNT: 106 THERE ARE 106 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L46 ANSWER 26 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:630575 HCAPLUS

DOCUMENT NUMBER: 130:249

TITLE: Antitumor activity of bax and p53 naked gene transfer in lung cancer: in vitro and in vivo analysis

AUTHOR(S): Coll, Jean-Luc; Negoescu, Adrien; Louis, Nathalie; Sachs, Laurent; Tenaud, Corine; Girardot,

Valerie; Demeinex, Barbara; Brambilla, Elisabeth;
Brambilla, Christian; **Favrot, Marie**
CORPORATE SOURCE: Lung Cancer Research Group, Institut Albert Bonniot,
Faculthd de Medecine, Universite Joseph Fourier,
Grenoble, 38706, Fr.
SOURCE: Human Gene Therapy (1998), 9(14), 2063-2074
CODEN: HGTHE3; ISSN: 1043-0342
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In vitro and in vivo data have demonstrated that virus-mediated p53 gene transfer can induce active cell death and lung tumor regression. In contrast, the therapeutic potential of bax, another apoptosis-inducing gene, has not been described. We compared p53 and bax cytotoxic effects by transient transfection of an average of 25±5% of the H-322 and H-358 bronchioloalveolar carcinoma cell lines in vitro. Under these conditions, bax expression killed 70 to 90% of the transfected cells whereas p53 killed only 40% of them. The killing activity of both genes involved apoptosis, as shown by TUNEL staining. Surprisingly, BrdU incorporation indicated that the cells that did resist Bax toxicity were blocked in the pre-S phase of the cell cycle, a result expected for p53 only. In vivo, repeated injections of naked DNA encoding Bax or p53 inhibited the growth of 4-mm pre-established H-322 tumors in nude mice. Growth retardation only, and not inhibition, was observed in H-358, a poorly transfectable and rapidly growing tumor. These results indicate that Bax and p53 share a similar, strong antitumor activity in vivo, even if the former is a more potent inducer of apoptosis in vitro.
CC 1-6 (Pharmacology)
Section cross-reference(s): 3
REFERENCE COUNT: 70 THERE ARE 70 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L46 ANSWER 27 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:395881 HCAPLUS
DOCUMENT NUMBER: 129:117313
TITLE: Cell death and cancer: replacement of apoptotic genes and inactivation of death suppressor genes in therapy
AUTHOR(S): **Favrot, M.; Coll, J. -L.**; Louis, N.; Negoescu, A.
CORPORATE SOURCE: Lung Cancer Research Group, Institut Albert Bonniot, Faculte de Medecine, Universite Joseph Fourier, Grenoble, 38706, Fr.
SOURCE: Gene Therapy (1998), 5(6), 728-739
CODEN: GETHEC; ISSN: 0969-7128
PUBLISHER: Stockton Press
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 218 refs. This review provides a critical evaluation of the increasing use of gene therapy in the treatment of malignancies to induce active cell death (ACD, apoptosis). This approach is consistent with the notion that cancer is an anomalous accumulation of cells largely resulting from diminished cell death. The review details the main genes potentially useful for therapy. Among these, p53 has received the majority of the investigators' attention and provided encouraging results. Even greater hope is offered by newly tried direct inducers of apoptosis, such as bax, bclXs and caspases. Another fruitful direction is the association of apoptosis-inducing gene transfer with radio- and chemotherapy, which are also inducers of ACD. There is a delicate balance between cell gain through mitosis and cell loss in neoplasia because spontaneous apoptosis is widely present in tumors. In fact, the tumor environment favors

bystander cell killing which appears to be a fundamental mechanism insofar as the rate of observed cell mortality cannot be accounted for by the known methods of gene transduction with efficiencies far below 100%. We conclude that apoptosis offers a mainstream approach for cancer gene therapy since ACD is highly inducible and only limited gains in malignant cell apoptosis may displace tumors from growth to regression.

CC 1-0 (Pharmacology)

Section cross-reference(s): 3, 14

REFERENCE COUNT: 218 THERE ARE 218 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L46 ANSWER 28 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:711885 HCAPLUS

DOCUMENT NUMBER: 128:43491

TITLE: Long-term survival of immunocompetent rats with intraperitoneal colon carcinoma tumors using herpes simplex thymidine kinase/ganciclovir and IL-2 treatments

AUTHOR(S): Coll, J.-L.; Mesnil, M.; Lefebvre, M.-F.; Lancon, A.; Favrot, M. C.

CORPORATE SOURCE: Dep. Biol. Tumeurs, Cent. Leon Berard, Lyon, Fr.

SOURCE: Gene Therapy (1997), 4(11), 1160-1166

CODEN: GETHEC; ISSN: 0969-7128

PUBLISHER: Stockton

DOCUMENT TYPE: Journal

LANGUAGE: English

AB We evaluated the gain in long-term survival of BDIX rats bearing DHDProB colon cancer developed in the peritoneal cavity after in vivo therapy with the tk Gene and GCV. The sensitivity and the bystander effect of DHDProB cells stably transduced with the tk gene evaluated in vitro were low, as one tk+ cell killed two tk- cells. This correlated with the low ability of a fluorescent dye to diffuse through gap junctions. In vivo, more than 75% of tk-transduced cells were required and at least 100 mg/kg/day of GCV had to be injected no later than day 5 after tumor implantation to obtain a curative effect. A partial protection of the cured animals against rechallenge with the parental cells was also observed. Based on these results, a protocol of i vivo gene therapy was designed in which the tk/GCV treatment was combined with IL-2 gene expression. When the tk- and IL-2 encoding plasmids were injected twice i.p. with DOTAP and the animals treated with GCV, three of five rats were cured. This antitumoral activity resulted from the combined toxic effects of DNA-DOTAP and tk/GCV plus a potential immune response mediated by IL-2.

CC 1-6 (Pharmacology)

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L46 ANSWER 29 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:125218 HCAPLUS

DOCUMENT NUMBER: 126:233175

TITLE: In vitro targeting and specific transfection of human neuroblastoma cells by chCE7 antibody-mediated gene transfer

AUTHOR(S): Coll, J.-L.; Wagner, E.; Combaret, V.; Metchler, K.; Amstutz, H.; Iacono-Di-Cacito, I.; Simon, N.; Favrot, M. C.

CORPORATE SOURCE: Centre Leon Berard, Lyon, Fr.

SOURCE: Gene Therapy (1997), 4(2), 156-161

CODEN: GETHEC; ISSN: 0969-7128

PUBLISHER: Stockton

DOCUMENT TYPE: Journal
LANGUAGE: English

AB We developed a new vector for gene targeting of neuroblastoma (NB) cells, based on the utilization of a monoclonal antibody (chCE7) covalently linked to polylysine (PL). In the presence of chloroquine, chCE7-PL-DNA complexes transfected NB cells as efficiently as DOTAP, transfectam, TF-X50 or lipofectamine. This was demonstrated by transfection of the luciferase of β -galactosidase reporter genes in three different NB cell lines. This transfection was specific, since it was inhibited in the presence of competing unconjugated chCE7 antibody (Ab), and was not observed in cell lines neg. for the CE7 antigen. We tested the potential biol. activity of a plasmid coding for γ -interferon (γ IFN) transfected with chCE7-PL. HLA ABC expression on NB cells was induced after transfection with pCMV- γ IFN at a higher level than after incubation with 1000 IU/mL of purified γ IFN. Moreover, these HLA ABC-pos. NB cells were able to activate autologous cytotoxic T lymphocytes in vitro. Thus chCE7-PL is able to target a plasmid to NB cells and to allow the expression of the transfected gene in a biol. active form.

CC 1-6 (Pharmacology)

L46 ANSWER 30 OF 30 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:899544 HCAPLUS
DOCUMENT NUMBER: 123:336763
TITLE: Expression of integrin and CD44 adhesion molecules on neuroblastoma: The relation to tumor aggressiveness and embryonic neural-crest differentiation
AUTHOR(S): Combaret, V.; Coll, J. L.; Favrot, M. C.
CORPORATE SOURCE: Laboratory Cell Biology, Centre Leon-Berard, Lyon, F-69373/08, Fr.
SOURCE: Invasion & Metastasis (1995), Volume Date 1994-1995, 14(1-6), 156-63
CODEN: INVMDJ; ISSN: 0251-1789
PUBLISHER: Karger
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review, with 50 refs. The immunohistol. expression of integrins and CD44 cell adhesion mol. was analyzed on neuroblastoma (NB) specimens to study the potential role of these mols. in normal differentiation and in the transformation of neural crest derivs. None of the specimens expressed the $\alpha 5\beta 1$ integrin heterodimer; the expression of $\alpha 3\beta 1$ heterodimer was maintained during all stages of differentiation; $\alpha 1\beta 1$ heterodimer was expressed on undifferentiated neuroblasts and on Schwann cells, but was lost on ganglion cells. In contrast $\alpha 2\beta 1$, $\alpha 6\beta 1$, $\alpha 6\beta 4$ and $\alpha V\beta 1$ expression was usually restricted to cells differentiated in the Schwann cell lineage. $\alpha V\beta 3$ was expressed on tumors developed in the mediastinum. CD44 was strongly detected on differentiated ganglioneuroblastomas, stage 1 and 2 ganglioneuromas, as well as low-grade stage 4S NB and normal neuroblasts migrating in the fetal adrenal gland. CD44 expression was observed on Schwann cells and ganglion cells; in contrast, it was expressed on only 50% stage 3 and 4 undifferentiated NB. None of these specimens expressed exons V5, V7 or V6. In a few specimens, an intracellular expression of exons V8-V10 was observed in ganglion cells. The expression of CD44 on NB may reflect its pattern of expression on sympatho-adrenal precursors and arrest differentiation at these stages. Conversely, CD44 expression may be silenced during malignant transformation. Taken together, these results indicate that human NB express a number of different integrin receptors in vivo, with a changing pattern of cell-surface expression

reflecting the degree of differentiation in the malignant cell rather than tumor progression. In contrast with all previously described human tumors, the lack of CD44 expression in NB clearly correlates with tumor aggressiveness.

CC 15-0 (Immunohistochemistry)

STRUCTURE / TEXT SEARCH OF SEQUENCE

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=> d que nos L13

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L5      283 SEA FILE=REGISTRY ABB=ON  PLU=ON  RGDFK/SQEP
L6      72  SEA FILE=REGISTRY ABB=ON  PLU=ON  RGDYK/SQEP
L7      29659 SEA FILE=REGISTRY ABB=ON  PLU=ON  CYCLIC/NTE
L8      333 SEA FILE=REGISTRY ABB=ON  PLU=ON  (L5 OR L6) AND L7
L9      338 SEA FILE=REGISTRY ABB=ON  PLU=ON  L3 OR L8
L11     120 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L9
L17     35926 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ?INTEGRIN?/BI
L18     15515 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ?DOXORUBICIN?/BI
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=> d que nos L22

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L7      29659 SEA FILE=REGISTRY ABB=ON  PLU=ON  CYCLIC/NTE
L8      333 SEA FILE=REGISTRY ABB=ON  PLU=ON  (L5 OR L6) AND L7
L9      338 SEA FILE=REGISTRY ABB=ON  PLU=ON  L3 OR L8
L11     120 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L9
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=> d que nos L29

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 L8 333 SEA FILE=REGISTRY ABB=ON PLU=ON (L5 OR L6) AND L7
 L9 338 SEA FILE=REGISTRY ABB=ON PLU=ON L3 OR L8
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=> d que nos L30

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 L8 333 SEA FILE=REGISTRY ABB=ON PLU=ON (L5 OR L6) AND L7
 L9 338 SEA FILE=REGISTRY ABB=ON PLU=ON L3 OR L8
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 L8 333 SEA FILE=REGISTRY ABB=ON PLU=ON (L5 OR L6) AND L7
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=> d que nos L36

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L33 98 SEA FILE=REGISTRY ABB=ON PLU=ON KLAKKLAK/SQSP
L34 85 SEA FILE=HCAPLUS ABB=ON PLU=ON L33
L36 6 SEA FILE=HCAPLUS ABB=ON PLU=ON L34 AND L19

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L47 43 (L13 OR L21 OR L22 OR L29 OR L30 OR L32 OR L36) NOT L46

=> d ibib abs hitind hitrn hitstr L47 1-43

L47 ANSWER 1 OF 43 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:274581 HCAPLUS
DOCUMENT NUMBER: 144:484012
TITLE: A novel heterobifunctional linker for facile access to
bioconjugates
AUTHOR(S): Singh, Yashveer; Spinelli, Nicolas; Defrancq, Eric;
Dumy, Pascal
CORPORATE SOURCE: LEDSS, UMR CNRS 5616, ICMG FR 2607, Universite Joseph
Fourier, Grenoble, F 38041, Fr.
SOURCE: Organic & Biomolecular Chemistry (2006), 4(7),
1413-1419
CODEN: OBCRAK; ISSN: 1477-0520
PUBLISHER: Royal Society of Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A convenient synthesis of a novel heterobifunctional linker mol. is
described. The linker contains a thiol-reactive nitropyridyl disulfide
group (Npys) and an aldehyde-reactive aminooxy group with a propensity to
form disulfide and oxime linkages. The utility of the linker
mol. to cross-link different biomols. has been demonstrated by employing
it in the efficient preparation of a peptide-oligonucleotide conjugate. The
linker reported herein could be a useful tool for cross-coupling of
different but appropriately functionalized biomols.

CC 9-14 (Biochemical Methods)

Section cross-reference(s): 27, 33, 34

IT 76880-29-0 80366-85-4 388633-55-4 887321-82-6

RL: RCT (Reactant); RACT (Reactant or reagent)

(novel heterobifunctional linker for facile access to bioconjugates)

IT 79546-55-7P 887140-26-3P 887140-27-4P 887140-28-5P
887382-39-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)

(novel heterobifunctional linker for facile access to bioconjugates)

IT 388633-55-4

RL: RCT (Reactant); RACT (Reactant or reagent)

(novel heterobifunctional linker for facile access to bioconjugates)

IT 887140-26-3P 887140-27-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)

(novel heterobifunctional linker for facile access to bioconjugates)

IT 388633-55-4

RL: RCT (Reactant); RACT (Reactant or reagent)

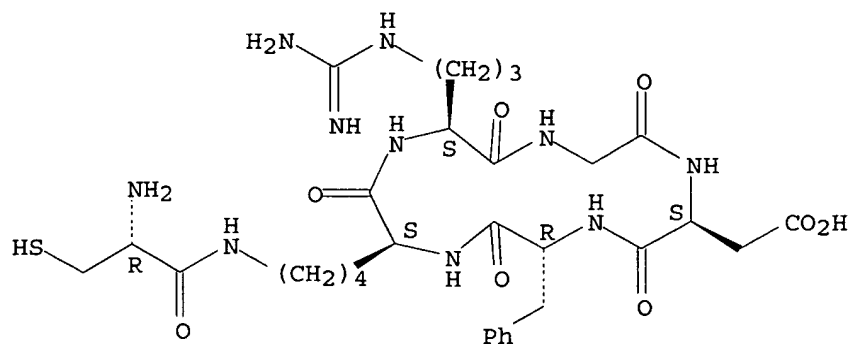
(novel heterobifunctional linker for facile access to bioconjugates)

RN 388633-55-4 HCAPLUS

CN Cyclo(L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-N⁶-L-cysteinyl-L-
lysyl) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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with
author
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IT 887140-26-3P 887140-27-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(novel heterobifunctional linker for facile access to bioconjugates)

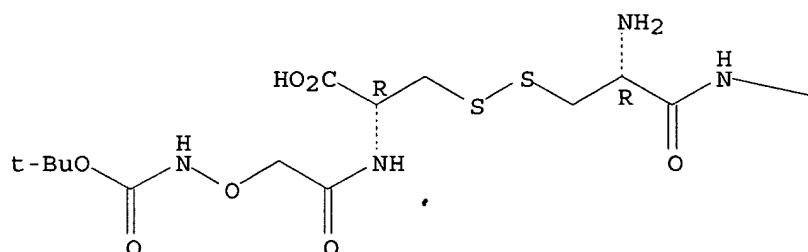
RN 887140-26-3 HCAPLUS

CN Cyclo(L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-N6-L-cysteinyl-L-lysyl), disulfide with N-[[[(1,1-dimethylethoxy)carbonyl]amino]oxy]acetyl]-L-cysteine (9CI) (CA INDEX NAME)

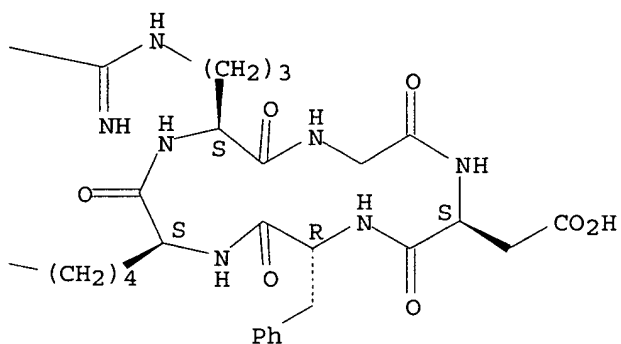
Absolute stereochemistry.

PAGE 1-A

H₂N—



PAGE 1-B



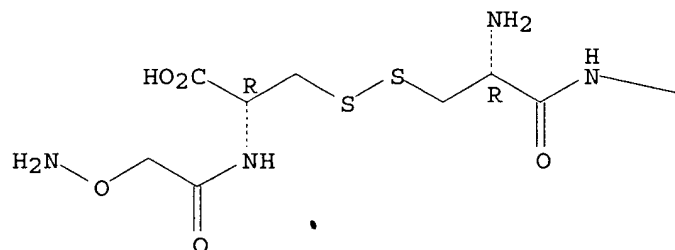
RN 887140-27-4 HCAPLUS

CN Cyclo(L-arginylglycyl-L-α-aspartyl-D-phenylalanyl-N6-L-cysteinyl-L-lysyl), disulfide with N-[(aminooxy)acetyl]-L-cysteine (9CI) (CA INDEX NAME)

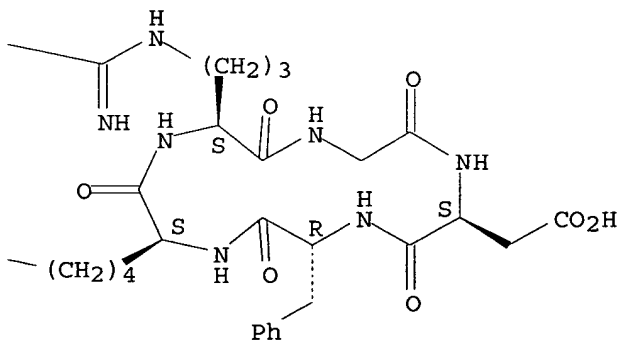
Absolute stereochemistry.

PAGE 1-A

H₂N



PAGE 1-B



REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

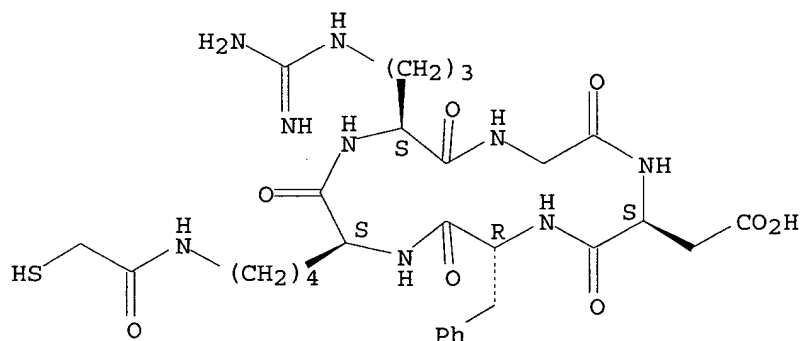
L47 ANSWER 2 OF 43 HCAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2005:1329578 HCAPLUS
 DOCUMENT NUMBER: 144:74804
 TITLE: Dual function polymer micelles used for drug delivery and contrast agents
 INVENTOR(S): Ai, Hua; Duerk, Jeffrey L.; Flask, Chris; Gao, Jinming; Lewin, Jonathan S.; Shuai, Xintao; Weinberg, Brent
 PATENT ASSIGNEE(S): Case Western Reserve University, USA
 SOURCE: PCT Int. Appl., 46 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005120585	A1	20051222	WO 2005-US19308	20050602
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

PRIORITY APPLN. INFO.: US 2004-577142P P 20040604
 AB The invention relates to micelles that are elaborated with functionality useful for imaging and/or selectively targeting tissue, e.g., in the delivery of hydrophobic agents. For example, micelles of diblock copolymer of ϵ -caprolactone and methoxy PEG was able to encapsulate antitumor agent **doxorubicin**.
 IC ICM A61K049-00
 CC 63-6 (Pharmaceuticals)
 Section cross-reference(s): 1, 15, 35
 ST polymer micelle drug delivery contrast agent; micelle caprolactone methoxy PEG diblock copolymer **doxorubicin** prepn antitumor
 IT **Integrins**
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 ($\alpha v \beta 3$, conjugates; dual function polymer micelles used for drug delivery and contrast agents)
 IT 23214-92-8, **DOXorubicin**
 RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (dual function polymer micelles used for drug delivery and contrast agents)
 IT 31054-18-9P **841255-57-0P** 871734-85-9P 871734-86-0P
 871734-87-1P 871734-88-2P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (dual function polymer micelles used for drug delivery and contrast

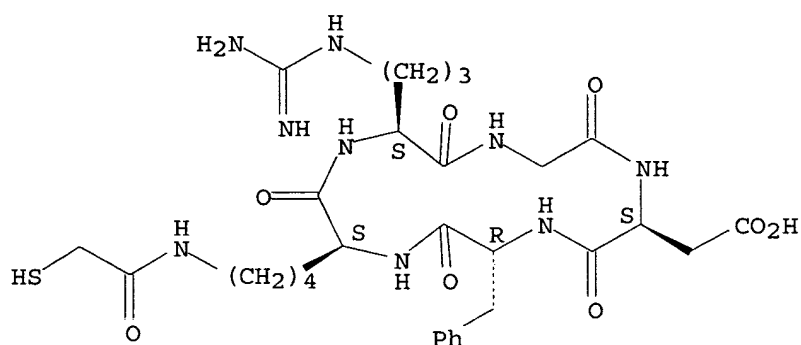
- agents)
- IT 250580-74-6P 698366-49-3P **841255-57-ODP**, reaction products with polymers 871734-85-9DP, reaction products with RGD derivs.
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(dual function polymer micelles used for drug delivery and contrast agents)
- IT **841255-57-OP**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(dual function polymer micelles used for drug delivery and contrast agents)
- IT **841255-57-ODP**, reaction products with polymers
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(dual function polymer micelles used for drug delivery and contrast agents)
- IT **841255-57-OP**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(dual function polymer micelles used for drug delivery and contrast agents)
- RN 841255-57-0 HCAPLUS
- CN Cyclo[L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-N6-(mercaptoacetyl)-L-lysyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



- IT **841255-57-ODP**, reaction products with polymers
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(dual function polymer micelles used for drug delivery and contrast agents)
- RN 841255-57-0 HCAPLUS
- CN Cyclo[L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-N6-(mercaptoacetyl)-L-lysyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 3 OF 43 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1228832 HCAPLUS

DOCUMENT NUMBER: 144:463348

TITLE: Quality analysis of in vivo near-infrared fluorescence and conventional gamma images acquired using a dual-labeled tumor-targeting probe

AUTHOR(S): Houston, Jessica P.; Ke, Shi; Wang, Wei; Li, Chun; Sevick-Muraca, Eva M.

CORPORATE SOURCE: Photon Migration Laboratory, Texas A&M University, College Station, TX, 77842-3012, USA

SOURCE: Journal of Biomedical Optics (2005), 10(5), 054010/1-054010/11

CODEN: JBOPFO; ISSN: 1083-3668

PUBLISHER: SPIE-The International Society for Optical Engineering

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The cyclic peptide, cyclopentapeptide cyclo(lys-Arg-Gly-Asp-phe) (c(KRGDf)), which is known to target $\alpha v \beta 3$ **integrin**, is dual-labeled with a radiotracer, ¹¹¹indium, for gamma scintigraphy as well as with a near-IR dye, IRDye800, for continuous-wave (cw) imaging of $\alpha v \beta 3$ pos. human M21 melanoma in **xenografts**. Twenty-four hours after administration of the dual-labeled peptide at a dose equivalent to 90 μ Ci of ¹¹¹In and 5 nmol of near-IR (NIR) dye, whole-body gamma scintigraphy and cw imaging was conducted. Image acquisition time was 15 min for the gamma scintigraphy images and 800 ms for the optical images acquired using an NIR sensitive intensified charge-coupled device. The results show that while the target-to-background ratio (TBR) of nuclear and optical imaging were similar for surface regions of interest and consistent with the origin of gamma and NIR radiation from a common targeted peptide, the signal-to-noise ratio (SNR) was significantly higher for optical than nuclear imaging. Furthermore, an anal. of SNR vs. contrast showed greater sensitivity of optical over nuclear imaging for the s.c. tumor targets. While tomog. reconstructions are necessary to probe TBR, SNR, and contrast for interior tissues, this work demonstrates for the first time the direct comparison of mol. optical and planar nuclear imaging for surface and subsurface cancers.

CC 8-9 (Radiation Biochemistry)

IT 161552-03-ODP, Indium-111-DTPA-IRDye800 labeled

RL: DGN (Diagnostic use); PKT (Pharmacokinetics); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses) (quality anal. of in vivo near-IR fluorescence and conventional gamma

images acquired using dual-labeled tumor-targeting probe)

IT 67-43-6, DTPA 15750-15-9, Indium-111, reactions 161552-03-0
211380-08-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(quality anal. of in vivo near-IR fluorescence and conventional gamma
images acquired using dual-labeled tumor-targeting probe)

IT 161552-03-ODP, DTPA derivs., IRDye800 labeled
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(quality anal. of in vivo near-IR fluorescence and conventional gamma
images acquired using dual-labeled tumor-targeting probe)

IT 161552-03-ODP, Indium-111-DTPA-IRDye800 labeled
RL: DGN (Diagnostic use); PKT (Pharmacokinetics); SPN (Synthetic
preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(quality anal. of in vivo near-IR fluorescence and conventional gamma
images acquired using dual-labeled tumor-targeting probe)

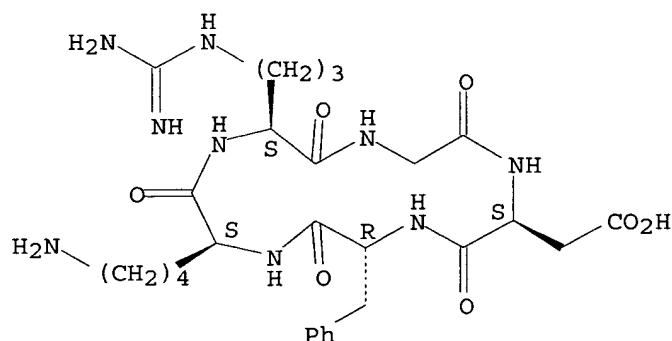
IT 161552-03-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(quality anal. of in vivo near-IR fluorescence and conventional gamma
images acquired using dual-labeled tumor-targeting probe)

IT 161552-03-ODP, DTPA derivs., IRDye800 labeled
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(quality anal. of in vivo near-IR fluorescence and conventional gamma
images acquired using dual-labeled tumor-targeting probe)

IT 161552-03-ODP, Indium-111-DTPA-IRDye800 labeled
RL: DGN (Diagnostic use); PKT (Pharmacokinetics); SPN (Synthetic
preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(quality anal. of in vivo near-IR fluorescence and conventional gamma
images acquired using dual-labeled tumor-targeting probe)

RN 161552-03-0 HCAPLUS
CN Cyclo(L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-L-lysyl) (9CI)
(CA INDEX NAME)

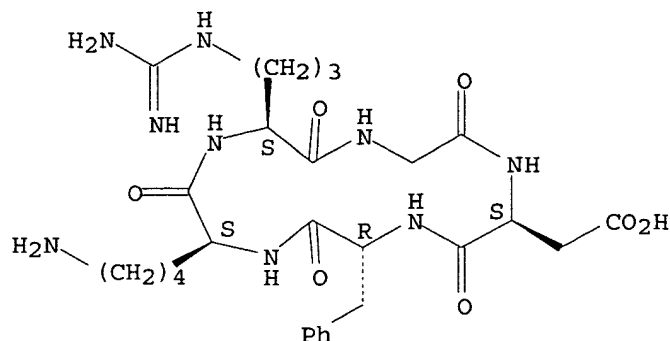
Absolute stereochemistry.



IT 161552-03-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(quality anal. of in vivo near-IR fluorescence and conventional gamma
images acquired using dual-labeled tumor-targeting probe)

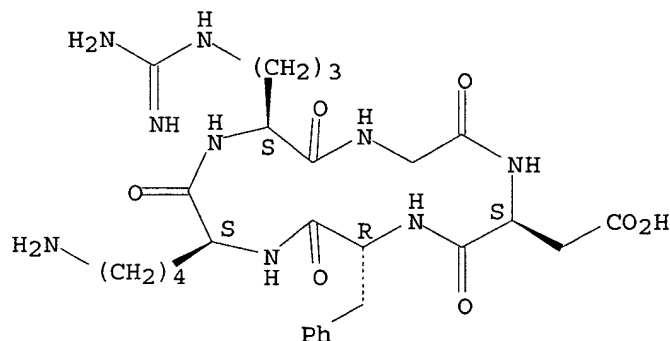
RN 161552-03-0 HCAPLUS
CN Cyclo(L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-L-lysyl) (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



IT 161552-03-0DP, DTPA derivs., IRDye800 labeled
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)
 (quality anal. of in vivo near-IR fluorescence and conventional gamma
 images acquired using dual-labeled tumor-targeting probe)
 RN 161552-03-0 HCAPLUS
 CN Cyclo(L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-L-lysyl) (9CI)
 (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 4 OF 43 HCAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2005:1155667 HCAPLUS
 DOCUMENT NUMBER: 144:66140
 TITLE: Near-Infrared Fluorescent RGD Peptides for Optical
 Imaging of **Integrin** $\alpha v \beta 3$
 Expression in Living Mice
 AUTHOR(S): Cheng, Zhen; Wu, Yun; Xiong, Zhengming; Gambhir,
 Sanjiv Sam; Chen, Xiaoyuan
 CORPORATE SOURCE: Molecular Imaging Program at Stanford (MIPS),
 Department of Radiology and Bio-X Program, Stanford
 University, Stanford, CA, 94305-5344, USA
 SOURCE: Bioconjugate Chemistry (2005), 16(6), 1433-1441
 CODEN: BCCHES; ISSN: 1043-1802
 PUBLISHER: American Chemical Society
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB Near-IR (NIR) fluorescence optical imaging is a powerful technique for
 studying diseases at the mol. level in preclin. models. The authors

recently reported that monomeric RGD peptide c(RGDyK) conjugated to the NIR fluorescent dye specifically targets **integrin** receptor both in cell culture and in living subjects. In this report, Cy5.5-conjugated mono-, di-, and tetrameric RGD peptides were evaluated in a s.c. U87MG glioblastoma **xenograft** model to investigate the effect of multimerization of RGD peptide on **integrin** avidity and tumor targeting efficacy. The binding affinities of Cy5.5-conjugated RGD monomer, dimer, and tetramer for $\alpha\beta3$ **integrin** expressed on U87MG cell surface were determined to be 42.9 ± 1.2 , 27.5 ± 1.2 , and 12.1 ± 1.3 nmol/L, resp. All three peptide-dye conjugates had **integrin** specific uptake both in vitro and in vivo. The s.c. U87MG tumor can be clearly visualized with each of these three fluorescent probes. Among them, tetramer displayed highest tumor uptake and tumor-to-normal tissue ratio from 0.5 to 4 h postinjection. Tumor-to-normal tissue ratio for Cy5.5-conjugated RGD monomer, dimer, and tetramer were 3.18 ± 0.16 , 2.98 ± 0.05 , and 3.63 ± 0.09 , resp., at 4 h postinjection. These results suggest that Cy5.5-conjugated monomeric, dimeric, and tetrameric RGD peptides are all suitable for **integrin** expression imaging. The multimerization of RGD peptide results in moderate improvement of imaging characteristics of the tetramer, compared to that of the monomer and dimeric counterparts.

CC 9-4 (Biochemical Methods)

Section cross-reference(s): 8

ST near IR fluorescent RGD peptide optical imaging **integrin**

alphavbeta3

IT RGD peptides

RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); SPN (Synthetic preparation); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)

(Cy5.5-conjugated; near-IR fluorescent RGD peptides for optical imaging of **integrin** $\alpha\beta3$ expression in living mice)

IT Human

Neuroglia, neoplasm

(glioblastoma; near-IR fluorescent RGD peptides for optical imaging of **integrin** $\alpha\beta3$ expression in living mice)

IT Affinity

Fluorescent indicators

Fluorometry

Imaging

Molecular association

Molecular recognition

(near-IR fluorescent RGD peptides for optical imaging of **integrin** $\alpha\beta3$ expression in living mice)

IT Fluorescence

(near-IR; near-IR fluorescent RGD peptides for optical imaging of **integrin** $\alpha\beta3$ expression in living mice)

IT **Integrins**

RL: ANT (Analyte); ANST (Analytical study)

($\alpha\beta3$; near-IR fluorescent RGD peptides for optical imaging of **integrin** $\alpha\beta3$ expression in living mice)

IT 172777-84-3P, Cy5.5

RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); SPN (Synthetic preparation); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)

(RGD peptide conjugates; near-IR fluorescent RGD peptides for optical imaging of **integrin** $\alpha\beta3$ expression in living mice)

IT 820967-21-3P 871583-34-5P 871702-39-5P

RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); SPN (Synthetic preparation); ANST (Analytical study); BIOL (Biological study);

PREP (Preparation); USES (Uses)

(near-IR fluorescent RGD peptides for optical imaging of
integrin $\alpha\beta 3$ expression in living mice)

IT 820967-21-3P 871583-34-5P 871702-39-5P

RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); SPN
(Synthetic preparation); ANST (Analytical study); BIOL (Biological study);
PREP (Preparation); USES (Uses)

(near-IR fluorescent RGD peptides for optical imaging of
integrin $\alpha\beta 3$ expression in living mice)

IT 820967-21-3P 871583-34-5P 871702-39-5P

RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); SPN
(Synthetic preparation); ANST (Analytical study); BIOL (Biological study);
PREP (Preparation); USES (Uses)

(near-IR fluorescent RGD peptides for optical imaging of
integrin $\alpha\beta 3$ expression in living mice)

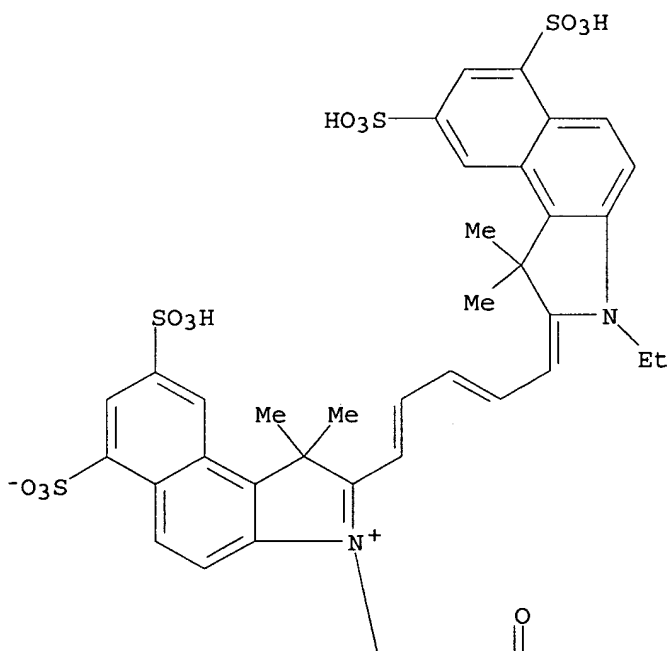
RN 820967-21-3 HCAPLUS

CN Cyclo[L-arginylglycyl-L- α -aspartyl-D-tyrosyl-N6-[6-[2-[5-(3-ethyl-
1,3-dihydro-1,1-dimethyl-6,8-disulfo-2H-benz[e]indol-2-ylidene)-1,3-
pentadienyl]-1,1-dimethyl-6,8-disulfo-1H-benz[e]indol-1-oxohexyl]-L-
lysyl], inner salt (9CI) (CA INDEX NAME)

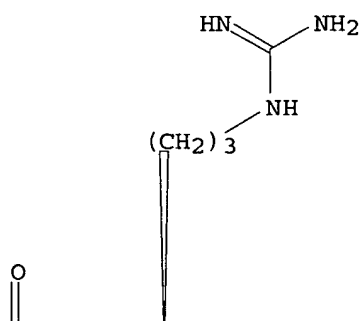
Absolute stereochemistry.

Double bond geometry unknown.

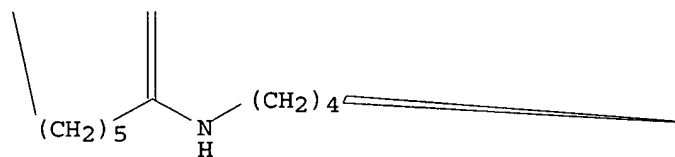
PAGE 1-A



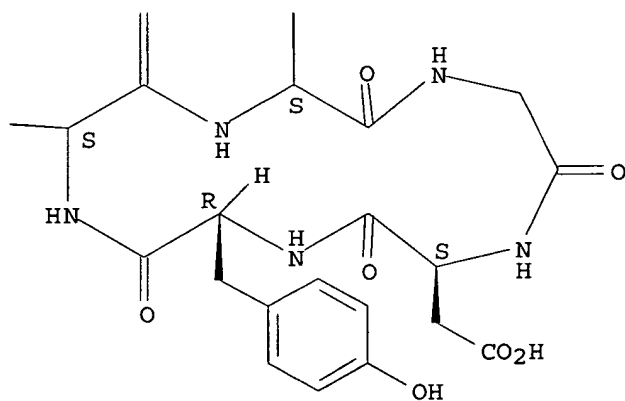
PAGE 1-B



PAGE 2-A



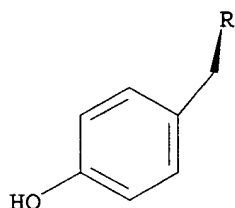
PAGE 2-B



RN 871583-34-5 HCAPLUS
CN Cyclo(L-arginylglycyl-L-α-aspartyl-D-tyrosyl-L-lysyl),

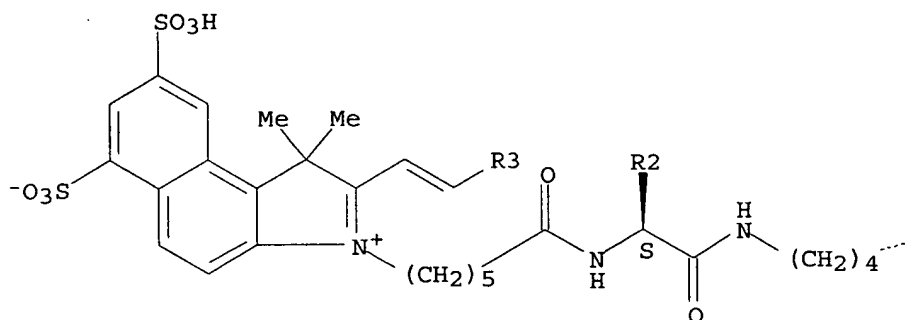
Absolute stereochemistry.
Double bond geometry unknown.

Chemical structure of a substituted indole derivative. The indole ring system has a methyl group (Me) at position 2, an ethyl group (Et) on the nitrogen, and a 2-sulfonylvinyl group at position 3. The 2-sulfonylvinyl group consists of a vinyl group (CH=CH-) attached to a sulfonyl group (SO₂-). The sulfonyl group is further substituted with a phenyl ring at the para position, which has two sulfonic acid groups (SO₃H) at the 3 and 5 positions. The R₃ group is attached to the terminal carbon of the vinyl group.

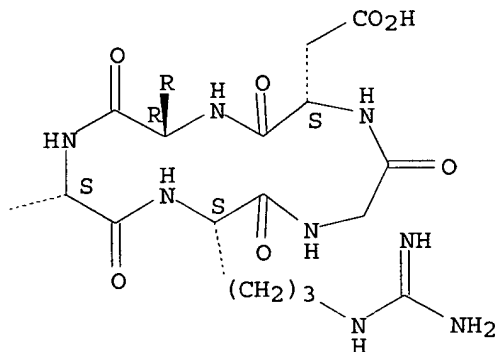


The chemical structure shows a macrocyclic compound with a 12-membered ring. The ring contains two amide bonds and two thioether linkages. Substituents include a 4-hydroxyphenyl group, a carboxylic acid group, and a guanidino group. A side chain with a terminal amide group is attached to the ring via a (CH₂)₄ linker. A label 'R2' with an arrow points to the bottom of the structure.

PAGE 3-A



PAGE 3-B



RN 871702-39-5 HCAPLUS

CN Cyclo(L-arginylglycyl-L- α -aspartyl-D-tyrosyl-L-lysyl),
 5,5',5'',5'''-[N-[6-[2-[5-(3-ethyl-1,3-dihydro-1,1-dimethyl-6,8-disulfo-2H-benz[e]indol-2-ylidene)-1,3-pentadienyl]-1,1-dimethyl-6,8-disulfo-1H-benz[e]indolio]-1-oxohexyl]-L-glutamoyl]bis[L-glutamoyl]bis-, inner salt
 (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 5 OF 43 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1138649 HCAPLUS

DOCUMENT NUMBER: 144:66024

TITLE: Effect of Coligands on Biodistribution Characteristics
 of Ternary Ligand 99mTc Complexes of a
 HYNIC-Conjugated Cyclic RGDfK Dimer

AUTHOR(S): Liu, Shuang; Hsieh, Wen-Yuan; Kim, Young-Seung;
 Mohammed, Sulma I.

CORPORATE SOURCE: Department of Industrial and Physical Pharmacy, School
 of Pharmacy, Purdue University, West Lafayette, IN,
 47907, USA

SOURCE: Bioconjugate Chemistry (2005), 16(6), 1580-1588

CODEN: BCCHES; ISSN: 1043-1802

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal
 LANGUAGE: English

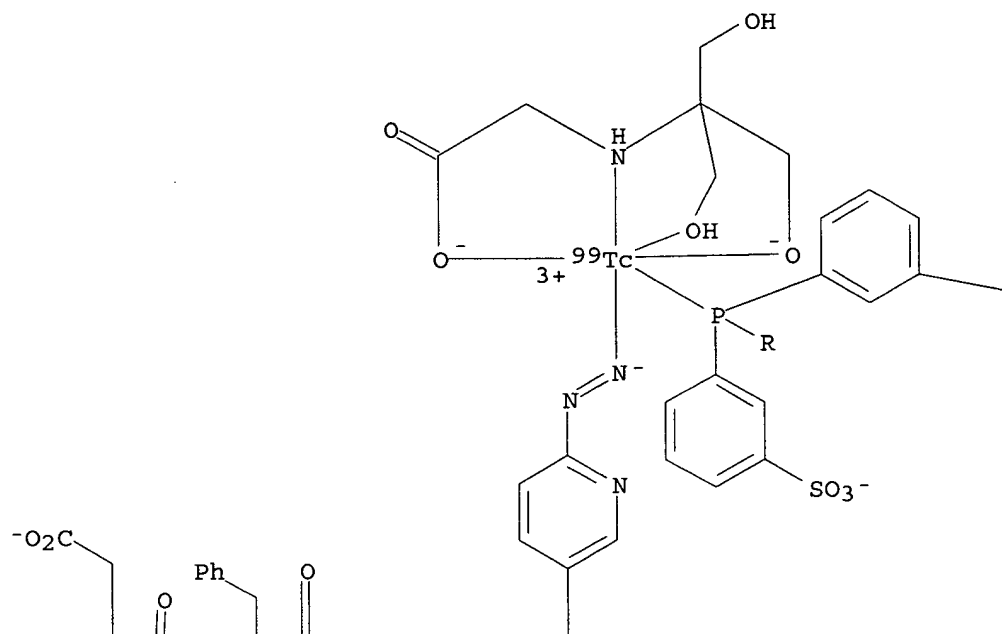
- AB This report describes biodistribution characteristics of three ternary ligand complexes [99mTc(SQ168)(tricine)(L)] (SQ168 = [2-[[[5-[carbonyl]-2-pyridinyl]hydrazono]methyl]-benzenesulfonic acid]-Glu(cyclo{Lys-Arg-Gly-Asp-D-Phe})-cyclo{Lys-Arg-Gly-Asp-D-Phe}); L = TPPTS (trisodium triphenylphosphine-3,3',3''-trisulfonate), ISONIC (isonicotinic acid) and PDA (2,5-pyridinedicarboxylic acid)) in athymic nude mice bearing MDA-MB-435 human breast cancer **xenografts**. Ternary ligand complexes [99mTc(SQ168)(tricine)(L)] (L = TPPTS, ISONIC and PDA) were prepared and were analyzed by a reversed HPLC method. Surprisingly, coligands have little impact on log P values of their ternary ligand 99mTc complexes even though HPLC retention times suggest that [99mTc(SQ168)(tricine)(PDA)] and [99mTc(SQ168)(tricine)(ISONIC)] are more hydrophilic than [99mTc(SQ168)(tricine)(TPPTS)]. The results from biodistribution studies indicated that excretion kinetics of the 99mTc-labeled cyclic RGDFK dimer can be modified by the choice of coligand. The fact that all three radiotracers show high tumor uptake during the 2 h study period suggests that the coligand has minimal effect on the tumor targeting capability of the 99mTc-labeled cyclic RGDFK dimer. Results from the blocking experiment suggest that the tumor localization of the 99mTc-labeled cyclic RGDFK dimer is **integrin** $\alpha v \beta 3$ -mediated. On the basis of their liver uptake and tumor/liver ratios, we believe that PDA has the advantage over TPPTS and ISONIC for the 99mTc-labeling of HYNIC-biomol. conjugates.
- CC 8-9 (Radiation Biochemistry)
- IT 250614-55-2P 871810-19-4P 871810-20-7P
 RL: DGN (Diagnostic use); PKT (Pharmacokinetics); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (coligands effect on biodistribution of ternary ligand 99mTc complexes of HYNIC-conjugated cyclic RGDFK dimer)
- IT 55-22-1, Isonicotinic acid, reactions 499-81-0, 3,5-Pyridinedicarboxylic acid 5704-04-1, Tricine 23288-60-0, Sodium pertechnetate-99Tc 63995-70-0, TPPTS 161552-03-0 186305-11-3 246234-73-1
 250612-45-4
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (coligands effect on biodistribution of ternary ligand 99mTc complexes of HYNIC-conjugated cyclic RGDFK dimer)
- IT 250612-47-6P 354815-20-6P, SQ 168
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (coligands effect on biodistribution of ternary ligand 99mTc complexes of HYNIC-conjugated cyclic RGDFK dimer)
- IT 250614-55-2P 871810-19-4P 871810-20-7P
 RL: DGN (Diagnostic use); PKT (Pharmacokinetics); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (coligands effect on biodistribution of ternary ligand 99mTc complexes of HYNIC-conjugated cyclic RGDFK dimer)
- IT 161552-03-0 250612-45-4
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (coligands effect on biodistribution of ternary ligand 99mTc complexes of HYNIC-conjugated cyclic RGDFK dimer)
- IT 250612-47-6P 354815-20-6P, SQ 168
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (coligands effect on biodistribution of ternary ligand 99mTc complexes of HYNIC-conjugated cyclic RGDFK dimer)
- IT 250614-55-2P 871810-19-4P 871810-20-7P
 RL: DGN (Diagnostic use); PKT (Pharmacokinetics); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)

(coligands effect on biodistribution of ternary ligand ^{99m}Tc complexes
of HYNIC-conjugated cyclic RGDfK dimer)

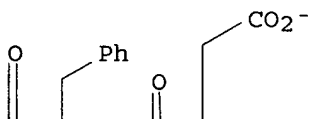
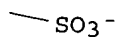
RN 250614-55-2 HCAPLUS

CN Technetate(5-)- ^{99}Tc , [[5,5'-[N-[[6-(diazenyl- $\kappa\text{N}2$)-3-pyridinyl]carbonyl]-L-glutamoyl]bis[cyclo(L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-L-lysylato)]](3-)] [N-[2-hydroxy-1,1-bis[(hydroxy- κO)methyl]ethyl]glycinato(2-)- $\kappa\text{N},\kappa\text{O}$][[3,3',3''-(phosphinidyne- κP)tris[benzenesulfonato]](3-)]-, trisodium dihydrogen (9CI) (CA INDEX NAME)

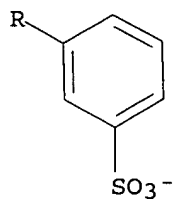
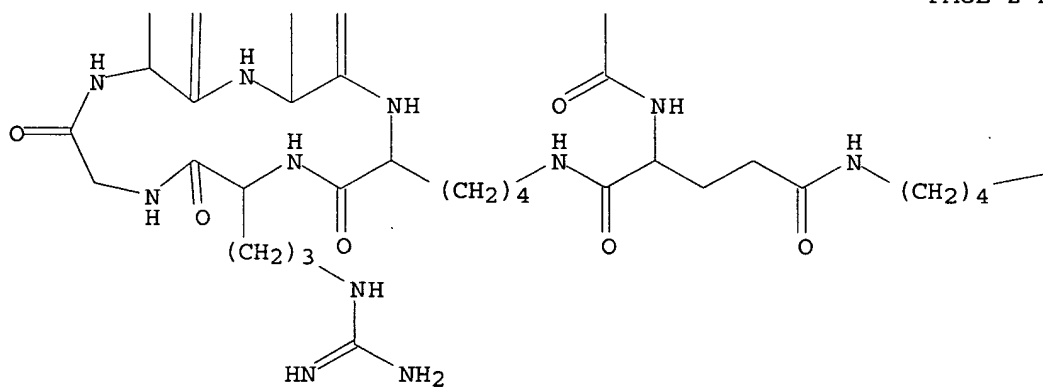
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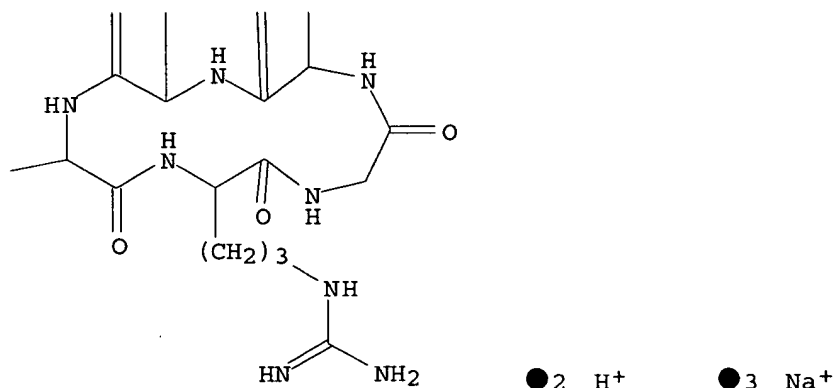
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PAGE 2-A



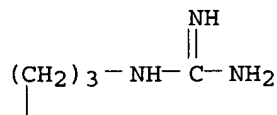
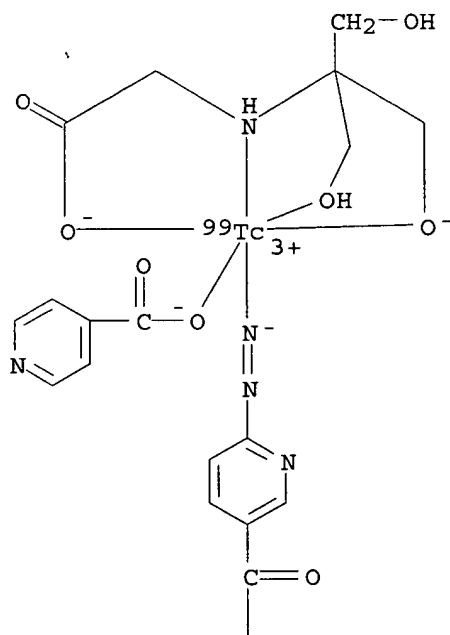
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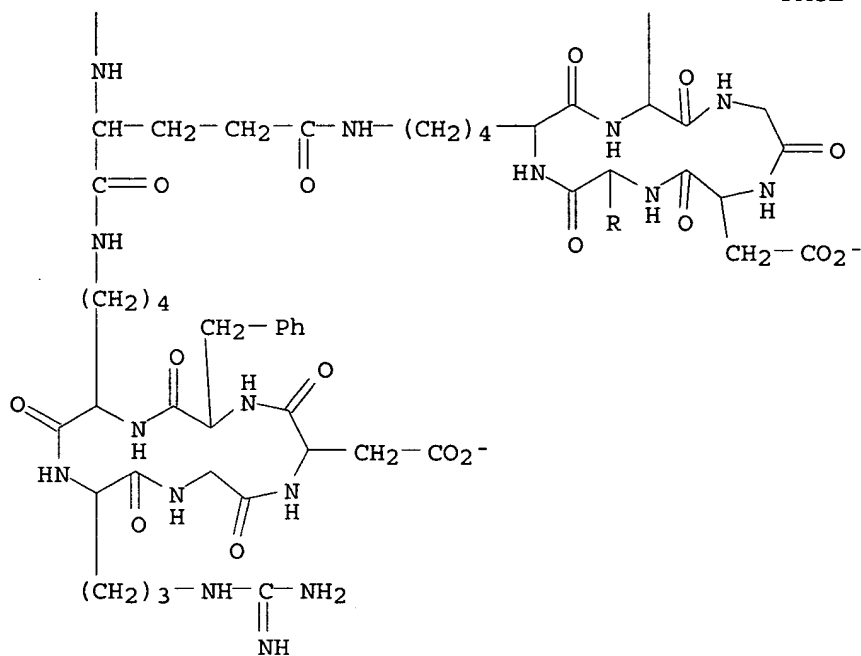
RN 871810-19-4 HCAPLUS

CN Technetate(3-)-99Tc, [5,5'-[N-[[6-(diazenyl-κN2)-3-pyridinyl]carbonyl]-L-glutamoyl]bis[cyclo(L-arginylglycyl-L-α-aspartyl-D-phenylalanyl-L-lysyl)]] [N-[2-(hydroxy-κO)-1-[(hydroxy-κO)methyl]-1-(hydroxymethyl)ethyl]glycinato(2-)-κN,κO] (4-pyridinecarboxylato-κO4)-, trihydrogen (9CI) (CA INDEX NAME)

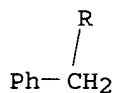
PAGE 1-A



PAGE 2-A



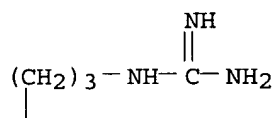
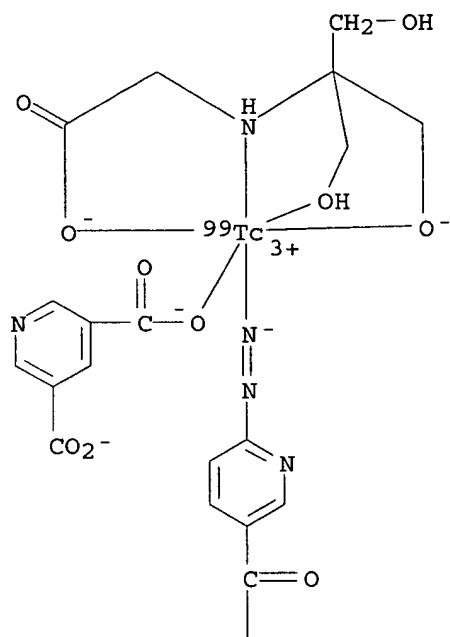
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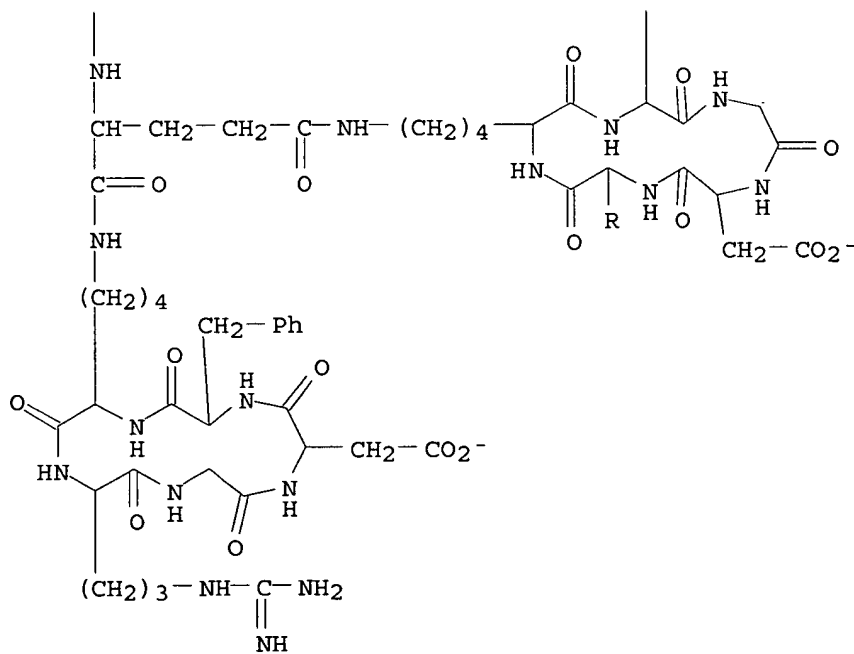
● 3 H^+

RN 871810-20-7 HCAPLUS
 CN Technetate(4-)-99Tc, [5,5'-[N-[[6-(diazanyl- $\kappa\text{N}2$)-3-pyridinyl]carbonyl]-L-glutamoyl]bis[cyclo(L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-L-lysyl)]] [N-[2-(hydroxy- κO)-1-[(hydroxy- κO)methyl]-1-(hydroxymethyl)ethyl]glycinato(2-)- $\kappa\text{N},\kappa\text{O}$](3,5-pyridinedicarboxylato- $\kappa\text{O}3$)-, tetrahydrogen (9CI) (CA INDEX NAME)

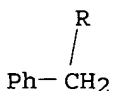
PAGE 1-A



PAGE 2-A



PAGE 3-A

● 4 H⁺

IT 161552-03-0 250612-45-4

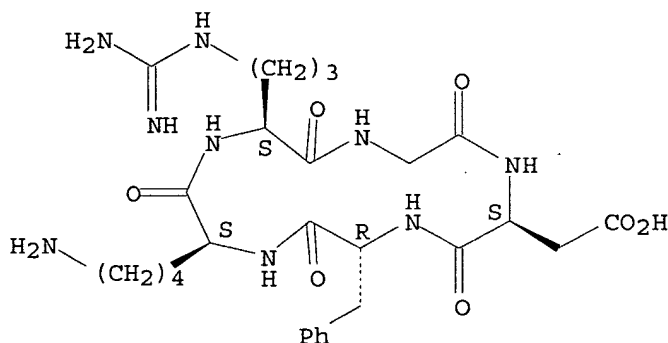
RL: RCT (Reactant); RACT (Reactant or reagent)

(coligands effect on biodistribution of ternary ligand 99mTc complexes
of HYNIC-conjugated cyclic RGDfK dimer)

RN 161552-03-0 HCAPLUS

CN Cyclo(L-arginylglycyl-L-α-aspartyl-D-phenylalanyl-L-lysyl) (9CI)
(CA INDEX NAME)

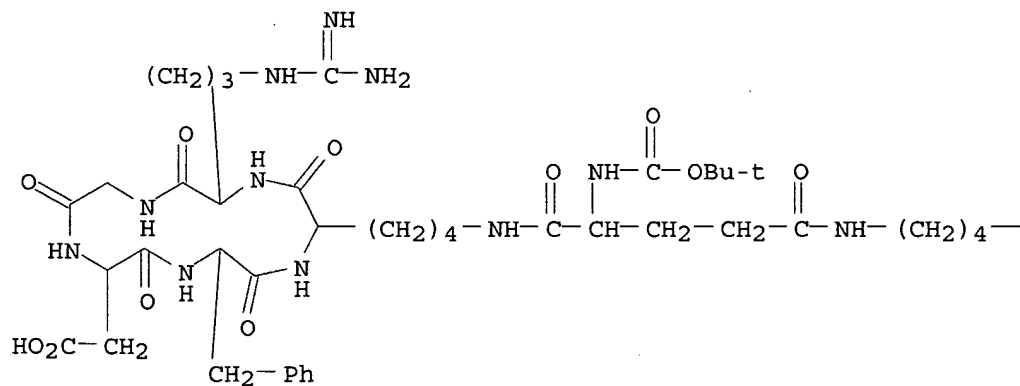
Absolute stereochemistry.



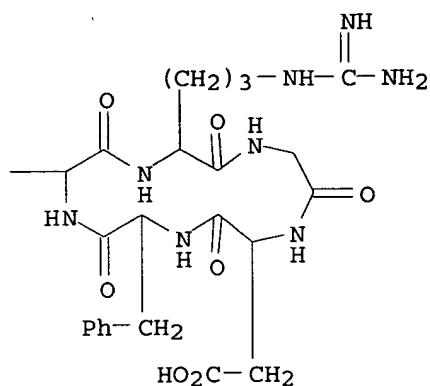
RN 250612-45-4 HCAPLUS

CN Cyclo(L-arginylglycyl-L-α-aspartyl-D-phenylalanyl-L-lysyl),
5,5'-[N-[(1,1-dimethylethoxy)carbonyl]-L-glutamoyl]bis- (9CI) (CA INDEX
NAME)

PAGE 1-A



PAGE 1-B



IT 250612-47-6P 354815-20-6P, SQ 168

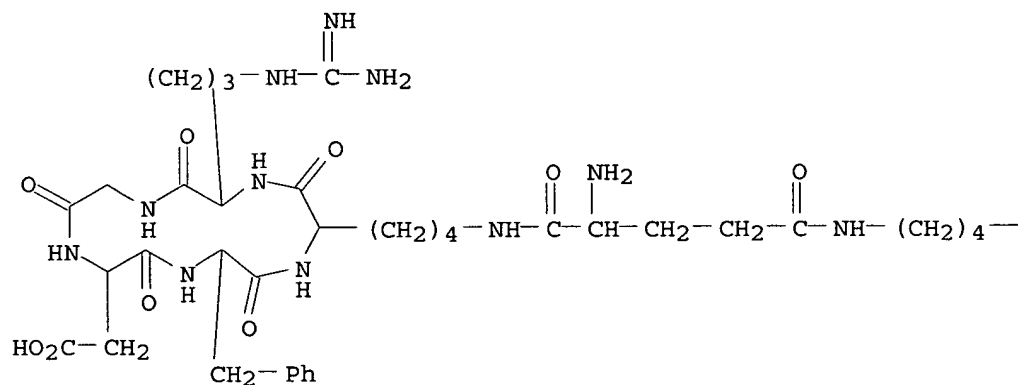
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(coligands effect on biodistribution of ternary ligand ^{99m}Tc complexes of HYNIC-conjugated cyclic RGDfK dimer)

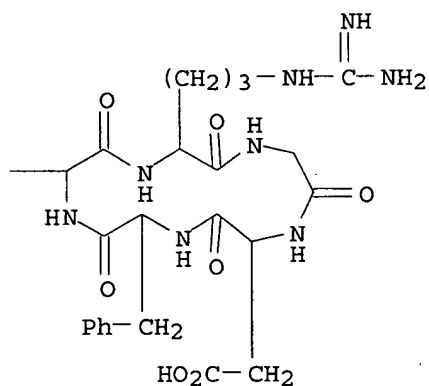
RN 250612-47-6 HCAPLUS

CN Cyclo(L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-L-lysyl),
5,5'-L-glutamoylbis- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B

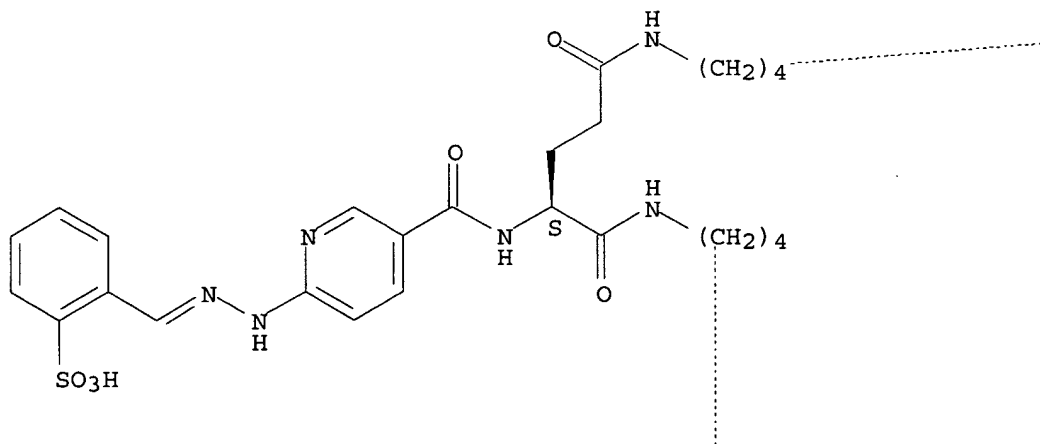


RN 354815-20-6 HCAPLUS

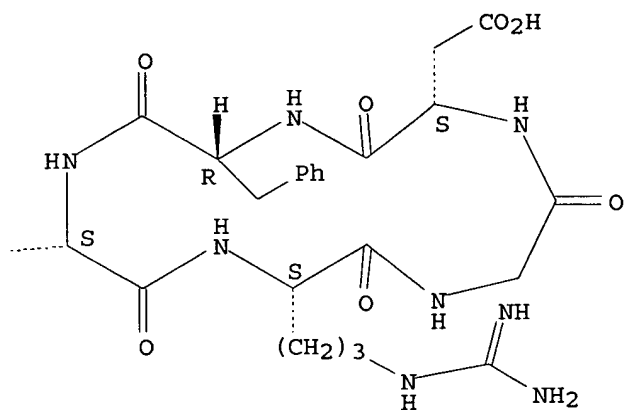
CN Cyclo(L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-L-lysyl),
5,5'-[N-[[6-[[[(2-sulfophenyl)methylene]hydrazino]-3-pyridinyl]carbonyl]-L-
glutamoyl]bis-, monosodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

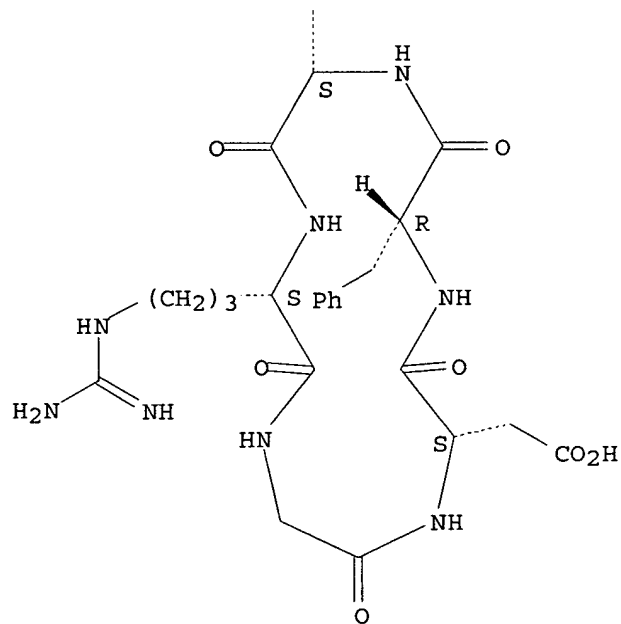
PAGE 1-A



PAGE 1-B



PAGE 2-A



PAGE 2-B

● Na

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 6 OF 43 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:694972 HCAPLUS

DOCUMENT NUMBER: 144:11467

TITLE: The effect of cyclo-DfKRG peptide immobilization on
titanium on the adhesion and differentiation of human
osteoprogenitor cells

AUTHOR(S): Pallu, Stephane; Bourget, Chantal; Bareille, Reine;
Labrugere, Christine; Dard, Michel; Sewing, Andreas;
Jonczyk, Alfred; Vernizeau, Michel; Durrieu, Marie
Christine; Amedee-Vilamitjana, Joelle

CORPORATE SOURCE: INSERM, U577, Universite Victor Segalen, Bordeaux,
F33076, Fr.

SOURCE: Biomaterials (2005), 26(34), 6932-6940

CODEN: BIMADU; ISSN: 0142-9612

PUBLISHER: Elsevier Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB This study takes place in the field of development of a bioactive surface
of titanium alloys. In this paper, titanium was functionalized with
cyclo-DfKRG peptide by coating or **grafting** using different
anchors (thiol or phosphonate) as spacers between the surface and the
peptide. Cell adhesion, and differentiation of human osteoprogenitor
(HOP) cells arising from human bone marrow were investigated. Our results
seem to demonstrate that cyclo-DfKRG peptide coating with a phosphonate
anchor and **grafting** procedure contributes to higher cell
adhesion and a strong ALP and Cbfa1 mRNA expression, after 10 days of cell
seeding. At the contrary, this peptide coated with a thiol anchor
stimulates differentiation of HOP within 3 days of culture.

CC 63-7 (Pharmaceuticals)

IT 12743-70-3, Ti6Al4V 15477-76-6, Phosphonate 181786-27-6

RL: BSU (Biological study, unclassified); PRP (Properties); THU

(Therapeutic use); BIOL (Biological study); USES (Uses)

(effect of cyclo-DfKRG peptide immobilization on titanium on adhesion
and differentiation of human osteoprogenitor cells)

IT 181786-27-6

RL: BSU (Biological study, unclassified); PRP (Properties); THU

(Therapeutic use); BIOL (Biological study); USES (Uses)

(effect of cyclo-DfKRG peptide immobilization on titanium on adhesion
and differentiation of human osteoprogenitor cells)

IT 181786-27-6

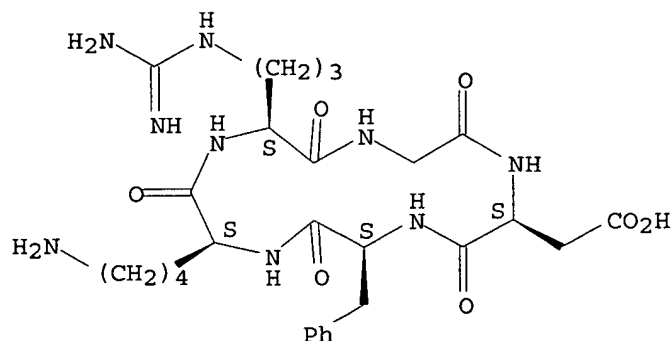
RL: BSU (Biological study, unclassified); PRP (Properties); THU

(Therapeutic use); BIOL (Biological study); USES (Uses)
(effect of cyclo-DfKRG peptide immobilization on titanium on adhesion
and differentiation of human osteoprogenitor cells)

RN 181786-27-6 HCAPLUS

CN Cyclo(L-arginylglycyl-L- α -aspartyl-L-phenylalanyl-L-lysyl) (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 7 OF 43 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:690681 HCAPLUS

DOCUMENT NUMBER: 143:323539

TITLE: A Bifunctional Targeted Peptide that Blocks HER-2
Tyrosine Kinase and Disables Mitochondrial Function in
HER-2-Positive Carcinoma Cells

AUTHOR(S): Fantin, Valeria R.; Berardi, Marcelo J.; Babbe,
Holger; Michelman, Montserrat V.; Manning, Charlene
M.; Leder, Philip

CORPORATE SOURCE: Department of Genetics, Harvard Medical School and
Howard Hughes Medical Institute, Boston, MA, USA

SOURCE: Cancer Research (2005), 65(15), 6891-6900
CODEN: CNREA8; ISSN: 0008-5472

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The HER-2 oncoprotein is commonly overexpressed in a variety of human malignancies and has become an attractive antitumor target. A number of strategies to inhibit the HER-2 receptor tyrosine kinase are currently the focus of intensive preclin. and clin. research. In the present study, we have engineered a bifunctional peptide, BHAP, which consists of two modular domains: a HER-2-targeting/neutralizing domain and a mitochondriotoxic, proapoptotic domain. The chimeric peptide is biol. active and capable of selectively triggering apoptosis of HER-2-overexpressing cancer cells in culture, even those previously described as Herceptin resistant. Furthermore, BHAP slows down growth of HER-2-overexpressing human mammary **xenografts** established in SCID mice. This approach can be extended to the development of tailored targeted chimeric peptides against a number of overexpressed cellular receptors implicated in the development and progression of cancer.

CC 14-1 (Mammalian Pathological Biochemistry)

Section cross-reference(s): 63

IT 865368-29-2

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)
(chimeric peptide to block HER-2 tyrosine kinase and mitochondrial activity in carcinoma cells)

IT 865368-29-2

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(chimeric peptide to block HER-2 tyrosine kinase and mitochondrial activity in carcinoma cells)

IT 865368-29-2

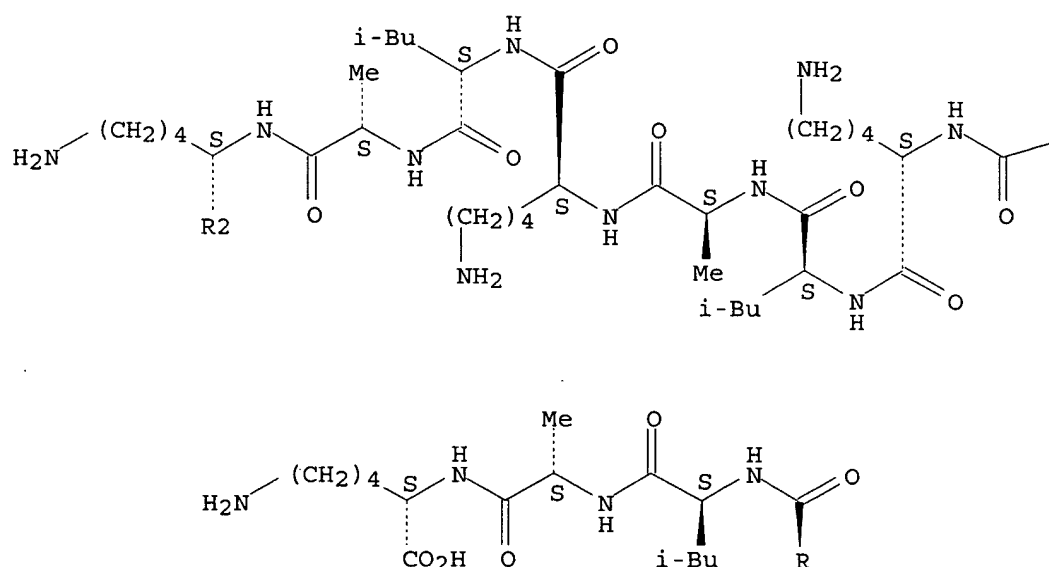
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(chimeric peptide to block HER-2 tyrosine kinase and mitochondrial activity in carcinoma cells)

RN 865368-29-2 HCAPLUS

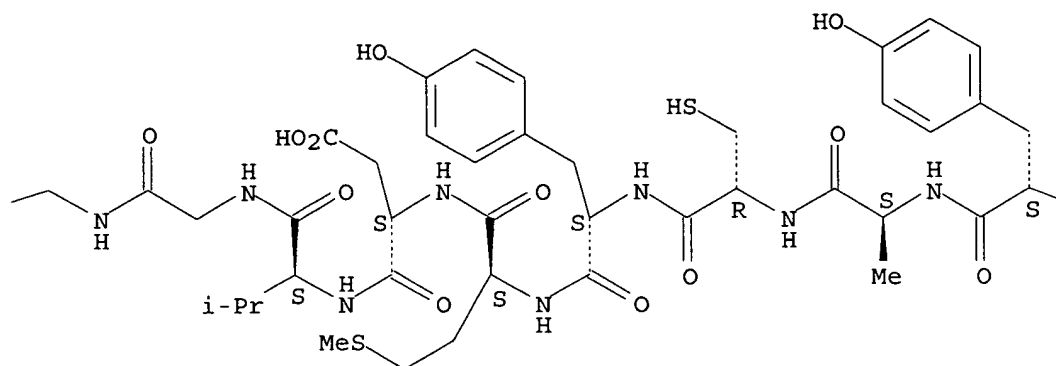
CN L-Lysine, L-tyrosyl-L-cysteinyl-L- α -aspartylglycyl-L-phenylalanyl-L-tyrosyl-L-alanyl-L-cysteinyl-L-tyrosyl-L-methionyl-L- α -aspartyl-L-valylglycylglycyl-L-lysyl-L-leucyl-L-alanyl-L-lysyl-L-leucyl-L-alanyl-L-lysyl-L-lysyl-L-leucyl-L-alanyl-L-lysyl-L-leucyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

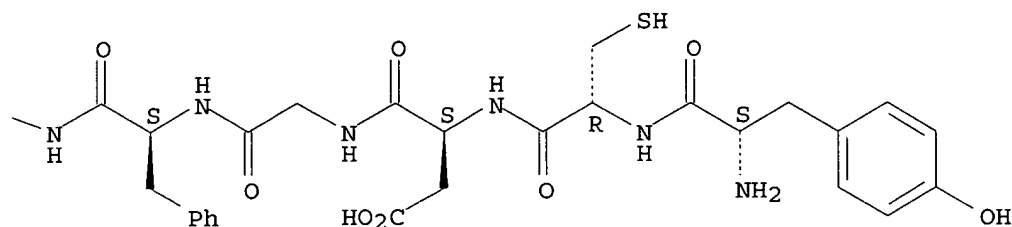
PAGE 1-A



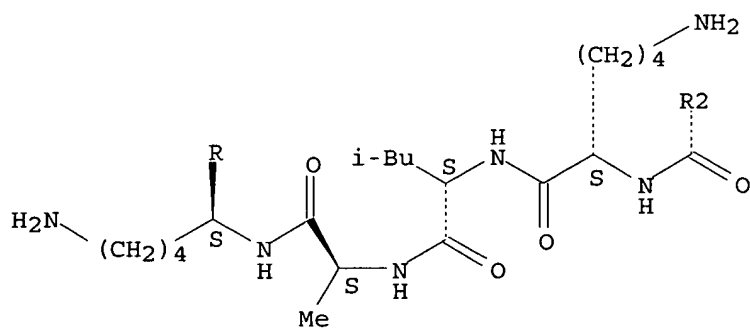
PAGE 1-B



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REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 8 OF 43 HCAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2005:638674 HCAPLUS
 DOCUMENT NUMBER: 143:146665
 TITLE: Compositions and methods of use of targeting peptides for diagnosis and therapy

INVENTOR(S): Pasqualini, Renata; Arap, Wadih; Kolonin, Mikhail;
Zurita, Amado J.
PATENT ASSIGNEE(S): Board of Regents, the University of Texas System, USA
SOURCE: PCT Int. Appl., 128 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005065418	A2	20050721	WO 2004-US44075	20041230
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

US 2005191294	A1	20050901	US 2004-26999	20041230
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PRIORITY APPLN. INFO.:	US 2003-533650P	P	20031231
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AB The compns. and methods include targeting peptides selective for tissue selective binding, particularly prostate and/or bone cancer, or adipose tissue. The methods may comprise targeting peptides that bind, for example, cell surface GRP78, IL-11R α in blood vessels of bone, or prohibitin of adipose vascular tissue. These peptides may be used to induce targeted apoptosis in the presence or absence of at least one pro-apoptotic peptide. Antibodies against such targeting peptides, the targeting peptides, or their mimeotopes may be used for detection, diagnosis and/or staging of a condition, such as prostate cancer or metastatic prostate cancer. Targeting peptide-pro-apoptotic peptide, CGRRAGGSC-GG-D(KLAKLAK)₂, bound specifically to IL-11R α and induced apoptosis in IL-11R α -pos. prostate cancer cell lines. It was also shown that ligand peptides to GRP78 (i) target prostate cancer cells in vitro, [ii] home to prostate cancer-derived **xenografts** in vivo, (iii) bind to human prostate cancer bone metastases and, when coupled to a pro-apoptotic peptide (iv) induce programmed cell death and (v) prevent tumor growth in a human prostate cancer **xenograft**. A peptide targeting prohibitin, when coupled with the pro-apoptotic peptide, not only prevented obesity development, but also caused a rapid decrease in white fat mass and obesity reversal.

IC ICM A61K

CC 1-6 (Pharmacology)

Section cross-reference(s): 9, 14, 15, 63

IT 859216-13-0 859216-14-1

RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(GRP78-targeted pro-apoptotic peptide; targeting peptides for diagnosis and therapy of prostate and/or bone cancer or adipose tissue targeting)

IT 859216-12-9

RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(prostate cancer targeting with; targeting peptides for diagnosis and

therapy of prostate and/or bone cancer or adipose tissue targeting)

IT 184240-26-4 404367-94-8 859509-00-5 859509-01-6
859624-99-0 859625-00-6
RL: PRP (Properties)
(unclaimed sequence; compns. and methods of use of targeting peptides
for diagnosis and therapy)

IT 859216-15-2
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);
PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES
(Uses)
(white fat vasculature-targeted pro-apoptotic peptide; targeting
peptides for diagnosis and therapy of prostate and/or bone cancer or
adipose tissue targeting)

IT 859216-13-0 859216-14-1
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);
PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES
(Uses)
(GRP78-targeted pro-apoptotic peptide; targeting peptides for diagnosis
and therapy of prostate and/or bone cancer or adipose tissue targeting)

IT 859216-12-9
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);
PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES
(Uses)
(prostate cancer targeting with; targeting peptides for diagnosis and
therapy of prostate and/or bone cancer or adipose tissue targeting)

IT 184240-26-4
RL: PRP (Properties)
(unclaimed sequence; compns. and methods of use of targeting peptides
for diagnosis and therapy)

IT 859216-15-2
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);
PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES
(Uses)
(white fat vasculature-targeted pro-apoptotic peptide; targeting
peptides for diagnosis and therapy of prostate and/or bone cancer or
adipose tissue targeting)

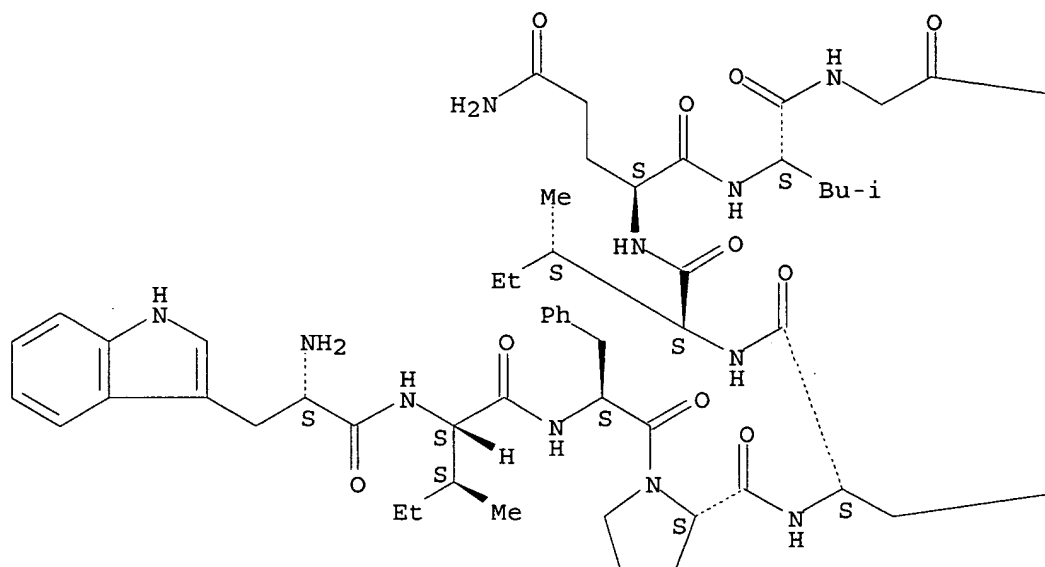
IT 859216-13-0 859216-14-1
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);
PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES
(Uses)
(GRP78-targeted pro-apoptotic peptide; targeting peptides for diagnosis
and therapy of prostate and/or bone cancer or adipose tissue targeting)

RN 859216-13-0 HCAPLUS

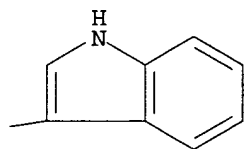
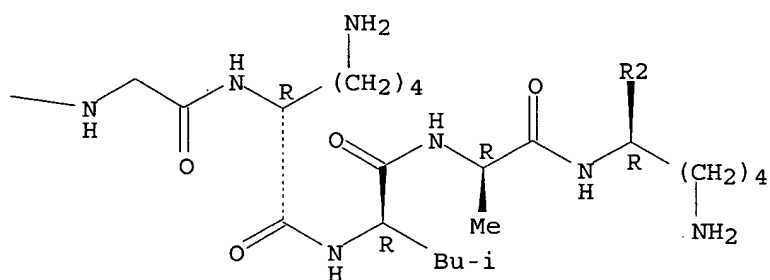
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isoleucyl-L-glutamyl-L-leucylglycylglycyl-D-lysyl-D-leucyl-D-alanyl-D-
lysyl-D-leucyl-D-alanyl-D-lysyl-D-lysyl-D-leucyl-D-alanyl-D-lysyl-D-leucyl-
D-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

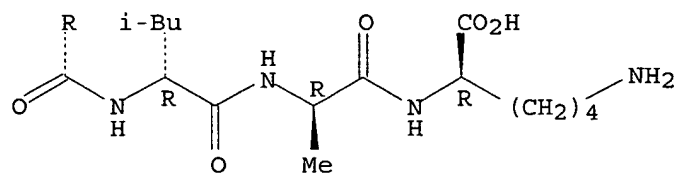
PAGE 1-A



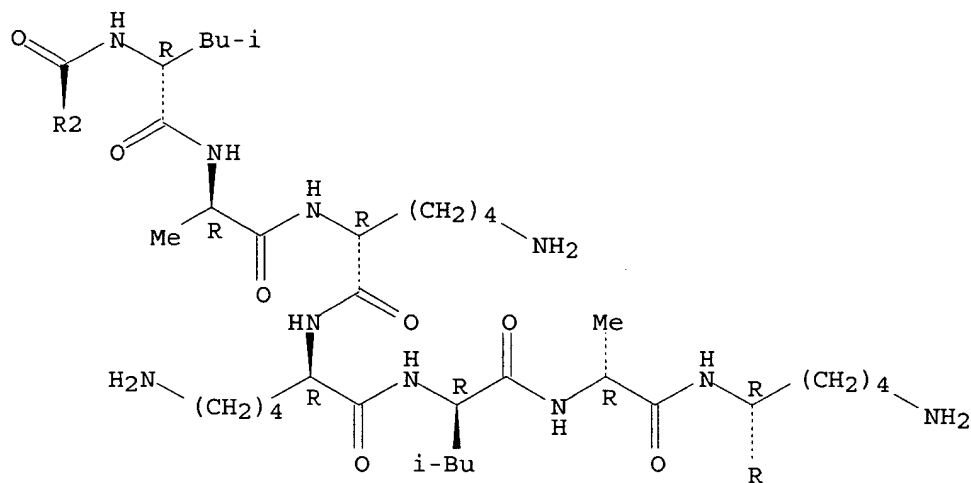
PAGE 1-B



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PAGE 3-A

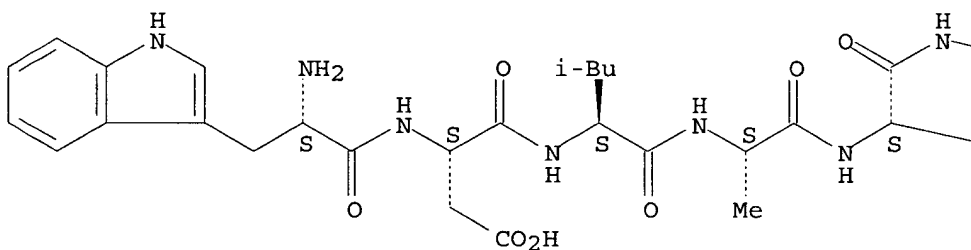


RN 859216-14-1 HCAPLUS

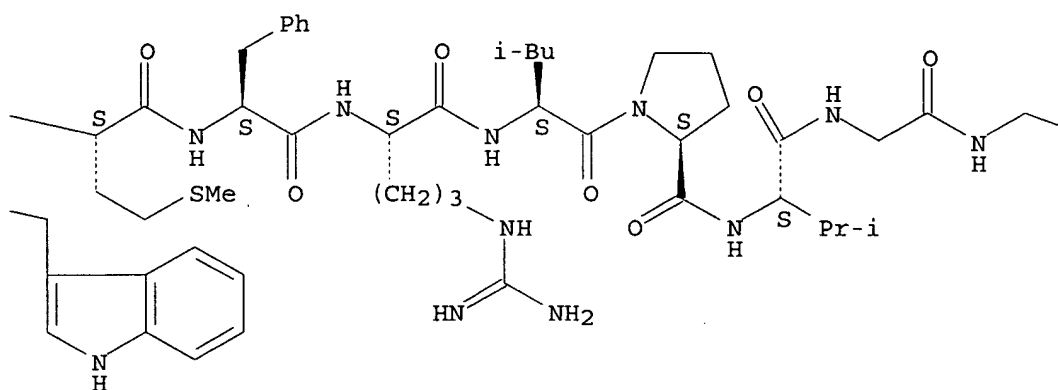
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Absolute stereochemistry.

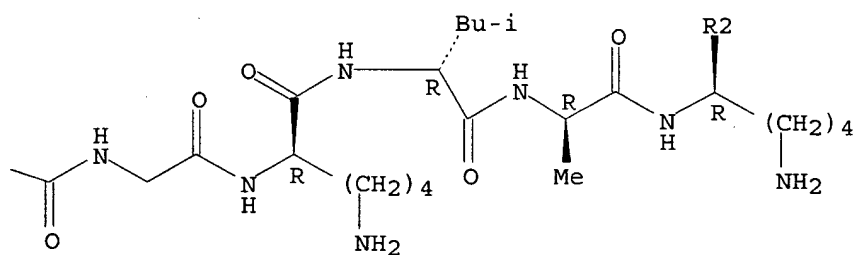
PAGE 1-A



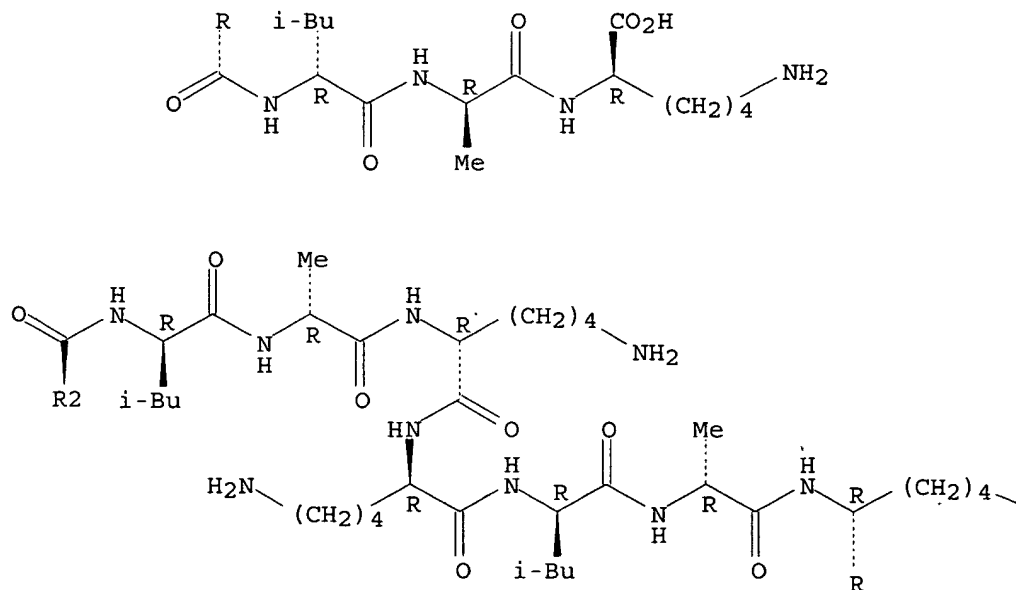
PAGE 1-B



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NH₂

IT 859216-12-9

RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);
PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES
(Uses)

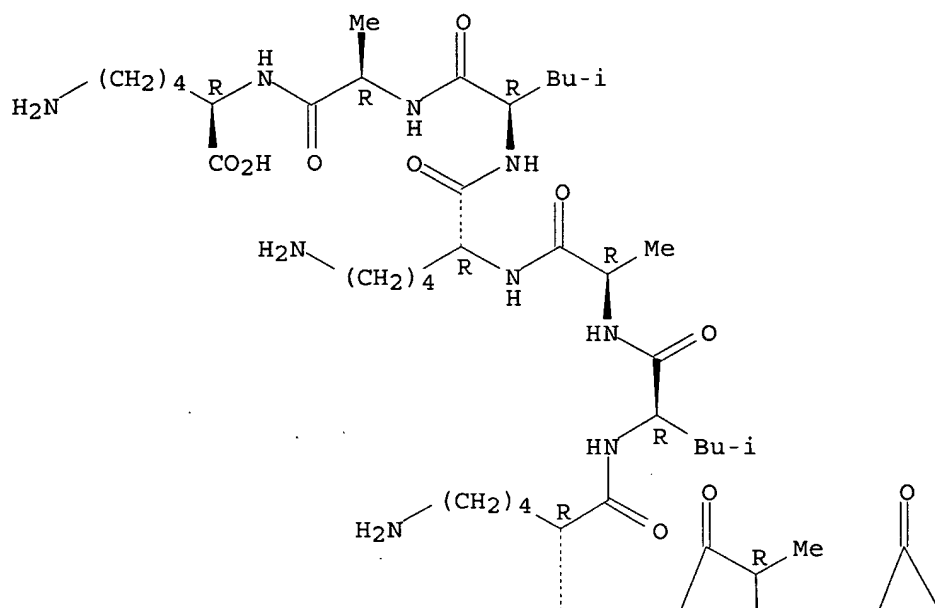
(prostate cancer targeting with; targeting peptides for diagnosis and
therapy of prostate and/or bone cancer or adipose tissue targeting)

RN 859216-12-9 HCAPLUS

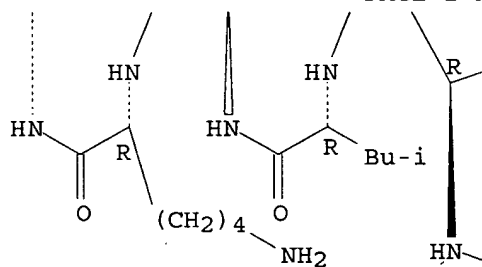
CN D-Lysine, L-cysteinyglycyl-L-arginyl-L-arginyl-L-alanylglycylglycyl-L-
seryl-L-cysteinyglycylglycyl-D-lysyl-D-leucyl-D-alanyl-D-lysyl-D-leucyl-D-
alanyl-D-lysyl-D-lysyl-D-leucyl-D-alanyl-D-lysyl-D-leucyl-D-alanyl- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

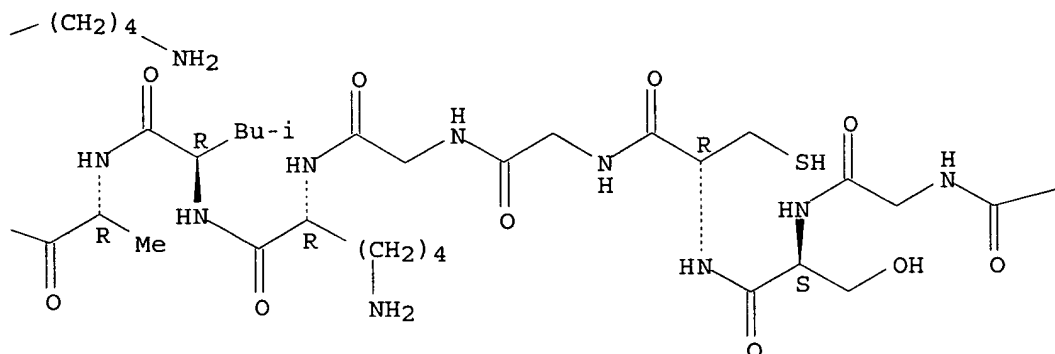
PAGE 1-A



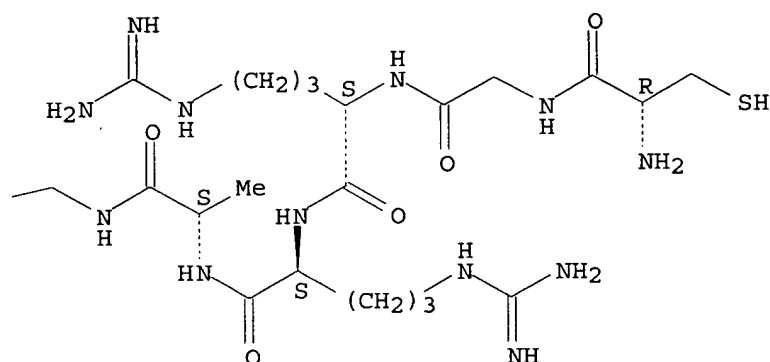
PAGE 2-A



PAGE 2-B



PAGE 2-C



IT 184240-26-4

RL: PRP (Properties)

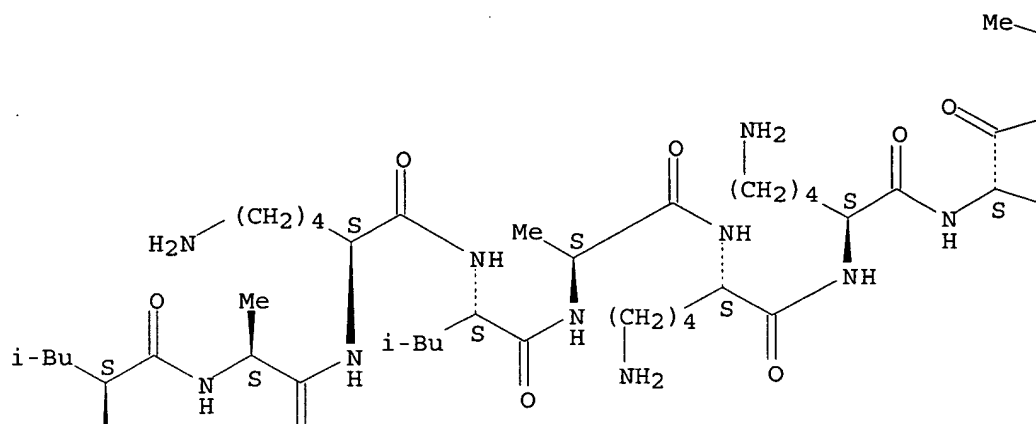
(unclaimed sequence; compns. and methods of use of targeting peptides for diagnosis and therapy)

RN 184240-26-4 HCAPLUS

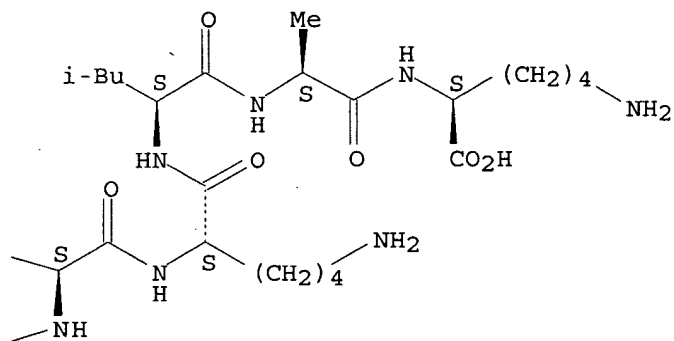
CN L-Lysine, L-lysyl-L-leucyl-L-alanyl-L-lysyl-L-leucyl-L-alanyl-L-lysyl-L-lysyl-L-leucyl-L-alanyl-L-lysyl-L-leucyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

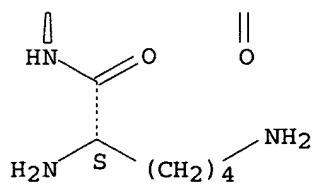


PAGE 1-B



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PAGE 2-A



IT 859216-15-2

RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);
PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES
(Uses)

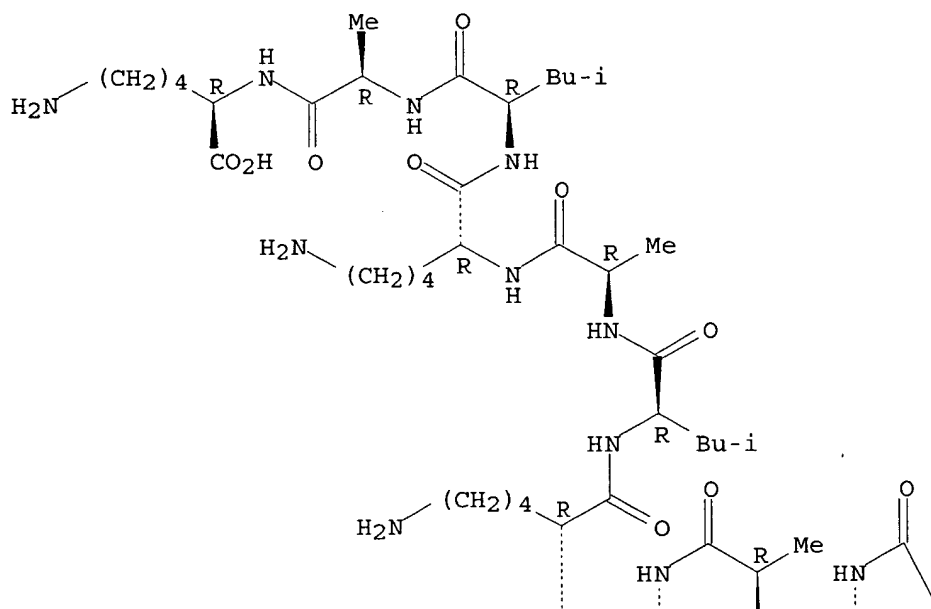
(white fat vasculature-targeted pro-apoptotic peptide; targeting
peptides for diagnosis and therapy of prostate and/or bone cancer or
adipose tissue targeting)

RN 859216-15-2 HCAPLUS

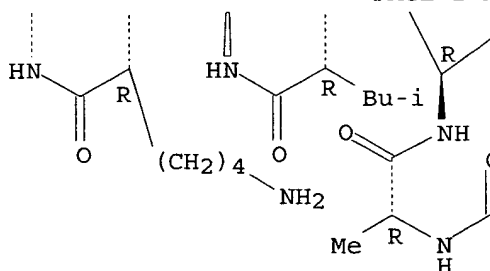
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D-leucyl-D-alanyl-D-lysyl-D-lysyl-D-leucyl-D-alanyl-D-lysyl-D-leucyl-D-
alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

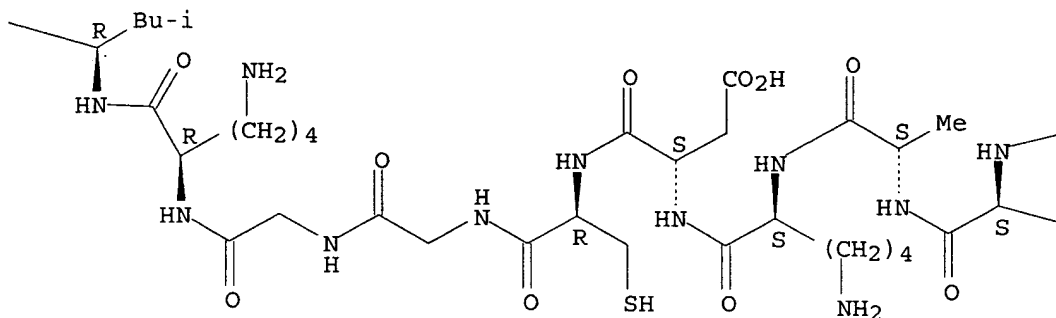
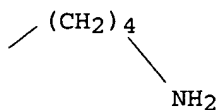
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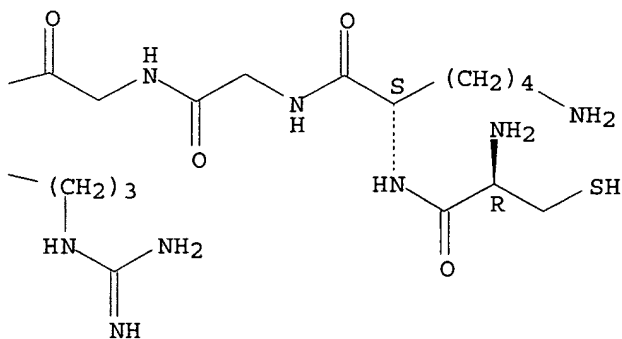
PAGE 2-A



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L47 ANSWER 9 OF 43 HCAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2005:599148 HCAPLUS
 DOCUMENT NUMBER: 144:307464
 TITLE: Quantifying molecular specificity of $\alpha\text{v}\beta 3$
integrin-targeted optical contrast agents with
 dynamic optical imaging
 AUTHOR(S): Gurfinkel, Michael; Ke, Shi; Wang, Wei; Li, Chun;
 Sevvick-Muraca, Eva M.
 CORPORATE SOURCE: Photon Migration Laboratories, Texas A&M University,
 College Station, TX, 77843-3012, USA
 SOURCE: Journal of Biomedical Optics (2005), 10(3),

034019/1-034019/9

CODEN: JBOPFO; ISSN: 1083-3668

PUBLISHER: SPIE-The International Society for Optical Engineering
 DOCUMENT TYPE: Journal
 LANGUAGE: English

- AB Dynamic fluorescence images were obtained from a s.c. human Kaposi's sarcoma tumor (KS1767) model immediately following the i.v. injection of an **integrin**-targeting cyanine dye conjugate, Cy5.5-c(KRGDf). The fluorescence images, acquired via an intensified charge-coupled device detection system, were used in conjunction with a pharmacokinetic (PK) model to determine kinetic properties of target binding in the presence and absence of a competitive ligand, free c(KRGDf). The results indicate that the conjugate dye behaves similarly in normal tissue to the free Cy5.5 dye while it possesses increased uptake in tumor tissue. The change in pharmacokinetic parameters obtained from dynamic imaging of Cy5.5-c(KRGDf) after administration of c(KRGDf) as a competitive ligand to the **integrin** receptor suggests that (i) the increased uptake of Cy5.5-c(KRGDf) is molecularly specific and that (ii) receptor turnover occurs within 24 h. In addition, PK anal. enables quantification of an in vivo c(KRGDf) binding constant attributable to **integrin** binding. In vivo pharmacokinetic anal. based on rapid and dynamic optical imaging may be potentially useful for evaluating the presence and turnover rate of disease markers that are potential targets of mol. medicine.
- CC 8-9 (Radiation Biochemistry)
 Section cross-reference(s): 14
- ST mol fluorescence imaging **integrin** receptor contrast agent tumor marker; fluorescent dye **integrin** receptor ligand conjugate tumor targeting
- IT Sarcoma
 (Kaposi's; dynamic fluorescence imaging of tumor model using **integrin**-targeting Cy5.5-c(KRGDf) cyanine dye)
- IT Pharmacokinetics
 (anal. of pharmacokinetics from dynamic fluorescence imaging of tumor model using **integrin**-targeting Cy5.5-c(KRGDf) cyanine dye)
- IT Imaging agents
 (contrast; quantifying mol. specificity of $\alpha\beta3$ **integrin**-targeted optical contrast agents with dynamic optical imaging)
- IT Cyanine dyes
 Human
 (dynamic fluorescence imaging of tumor model using **integrin**-targeting Cy5.5-c(KRGDf) cyanine dye)
- IT Imaging
 (fluorescent, dynamic; quantifying mol. specificity of $\alpha\beta3$ **integrin**-targeted optical contrast agents with dynamic optical imaging)
- IT Tumor markers
 (quantifying mol. specificity of $\alpha\beta3$ **integrin**-targeted optical contrast agents with dynamic optical imaging)
- IT Charge coupled devices
 (quantifying mol. specificity of $\alpha\beta3$ **integrin**-targeted optical contrast agents with dynamic optical imaging via intensified charge coupled devices)
- IT Imaging
 (tumor; dynamic fluorescence imaging of tumor model using **integrin**-targeting Cy5.5-c(KRGDf) cyanine dye)
- IT Biological transport
 (uptake; dynamic fluorescence imaging of tumor model using **integrin**-targeting Cy5.5-c(KRGDf) cyanine dye)
- IT Transplant and Transplantation

(xenotransplant; dynamic fluorescence imaging of tumor model on **xenografts** using **integrin**-targeting Cy5.5-c(KRGdf) cyanine dye)

IT **Integrins**

RL: ANT (Analyte); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)

($\alpha v \beta 3$; quantifying mol. specificity of $\alpha v \beta 3$

integrin-targeted optical contrast agents with dynamic optical imaging via intensified charge coupled devices)

IT **161552-03-0D**, conjugate with Cy5.5 172777-84-3D, Cy5.5, conjugate with peptide c(KRGDF)

RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PKT (Pharmacokinetics); BIOL (Biological study); USES (Uses)

(dynamic fluorescence imaging of tumor model using **integrin**

-targeting Cy5.5-c(KRGdf) cyanine dye)

IT **161552-03-0D**, conjugate with Cy5.5

RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PKT (Pharmacokinetics); BIOL (Biological study); USES (Uses)

(dynamic fluorescence imaging of tumor model using **integrin**

-targeting Cy5.5-c(KRGdf) cyanine dye)

IT **161552-03-0D**, conjugate with Cy5.5

RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PKT (Pharmacokinetics); BIOL (Biological study); USES (Uses)

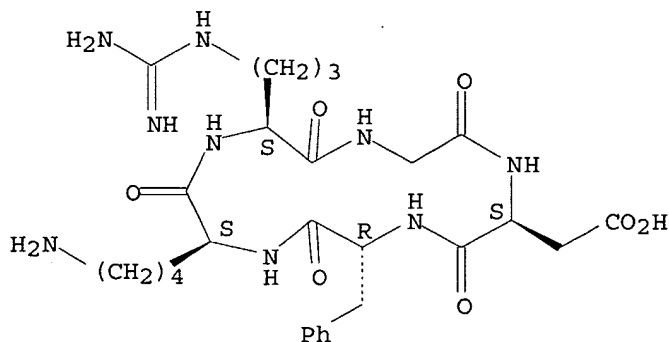
(dynamic fluorescence imaging of tumor model using **integrin**

-targeting Cy5.5-c(KRGdf) cyanine dye)

RN 161552-03-0 HCAPLUS

CN Cyclo(L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-L-lysyl) (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 10 OF 43 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:346801 HCAPLUS

DOCUMENT NUMBER: 142:411587

TITLE: Targeted drug-formaldehyde conjugates and methods of making and using the same

INVENTOR(S): Koch, Tad H.; Coleman, Michael P.; Cogan, Peter S.; Burke, Patrick J.; Post, Glen C.; Burkhart, David J.; McKenzie, Andrew R.; Jackson, Katrina L.; Kalet, Brian T.

PATENT ASSIGNEE(S): The Regents of the University of Colorado, USA

SOURCE: PCT Int. Appl., 180 pp.

CODEN: PIXXD2

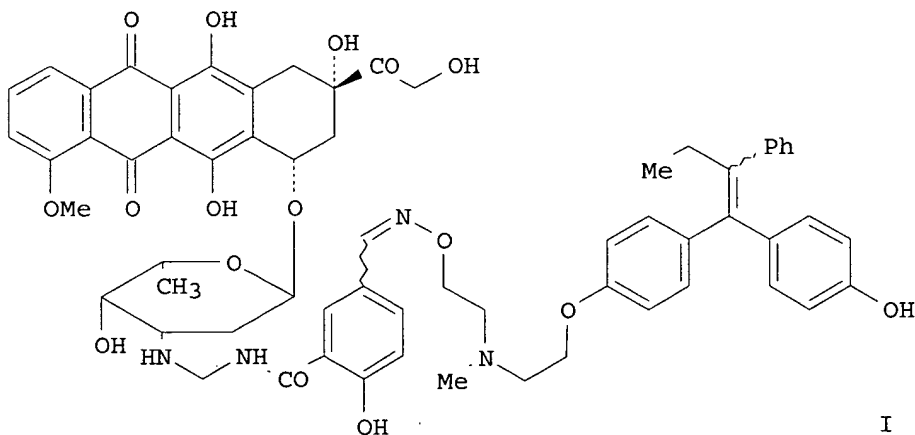
DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005034856	A2	20050421	WO 2004-US29095	20040907
WO 2005034856	A3	20050811		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-500608P P 20030905
 OTHER SOURCE(S): MARPAT 142:411587
 GI



AB This invention disclosed a prodrug platform technol. for improving the therapeutic value of a variety of parent drug compds. by altering and improving drug characteristics such as aqueous solubility, hydrolytic stability, therapeutic index, toxicity profile, pharmacokinetics and selectivity while allowing the potential for synthetic elaboration. The prodrug platform of the general form D-X-T (D = therapeutic drug moiety; X = linking moiety; T = biol. activity targeting moiety) is particularly well suited for targeting therapeutic drugs, including anti-tumor drugs and antibiotics, to specific receptors on target cells (e.g., cancer cells and bacteria). The platform is a technol. for providing an improved, pre-activated form of a therapeutic drug, and for optionally targeting such drug to target cells or biol. mols. Thus, the **oxime** prodrug I was prepared and consists of a **doxorubicin** antitumor

moiety tethered via a salicylamide moiety to a 4-hydroxytamoxifen estrogen receptor binding moiety. The invention is broadly applicable to many different therapeutic drugs, as well as to a variety of diseases and conditions, including a variety of forms of cancer and bacterial infections.

IC ICM A61K

CC 33-7 (Carbohydrates)

Section cross-reference(s): 1, 26, 34, 63

ST doxsaliform analog formaldehyde conjugate synthesis antitumor prodrug; doxorubicin analog formaldehyde conjugate synthesis antitumor prodrug; antibiotic prodrug formaldehyde conjugate synthesis; antibacterial prodrug formaldehyde conjugate synthesis; drug delivery system formaldehyde conjugate synthesis antitumor prodrug

IT Integrins

RL: BSU (Biological study, unclassified); BIOL (Biological study) ($\alpha v\beta 3$, antagonists; preparation of targeted drug-formaldehyde conjugates for therapeutic use as anticancer and antibiotic prodrugs)

IT 850256-67-6P 850256-68-7P 850256-69-8P 850256-70-1P

850410-56-9P 850410-58-1P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(claimed compound; preparation of targeted drug-formaldehyde conjugates for therapeutic use as anticancer and antibiotic prodrugs)

IT 65-45-2, Salicylamide 77-71-4 77-76-9, 2,2-Dimethoxypropane 103-65-1

106-93-4 110-52-1, 1,4-Dibromobutane 110-65-6, 2-Butyne-1,4-diol

110-85-0, Piperazine, reactions 111-46-6, reactions 112-27-6

141-75-3, Butanoyl chloride 540-51-2, 2-Bromoethanol 5414-19-7

25316-40-9, Doxorubicin hydrochloride 29022-11-5 31255-10-4

32780-64-6, Labetalol hydrochloride 35661-40-6 36894-69-6, Labetalol

42989-85-5 61002-54-8 71989-14-5 85721-33-1, Ciprofloxacin

92619-32-4 102273-25-6 103213-32-7 119062-05-4 135248-89-4

154445-77-9 194853-86-6 198139-51-4, Oregon Green 488 carboxylic acid

succinimidyl ester 214750-77-3 783289-63-4 850256-37-0

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of targeted drug-formaldehyde conjugates for therapeutic use as anticancer and antibiotic prodrugs)

IT 850256-67-6P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(claimed compound; preparation of targeted drug-formaldehyde conjugates for therapeutic use as anticancer and antibiotic prodrugs)

IT 850256-67-6P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(claimed compound; preparation of targeted drug-formaldehyde conjugates for therapeutic use as anticancer and antibiotic prodrugs)

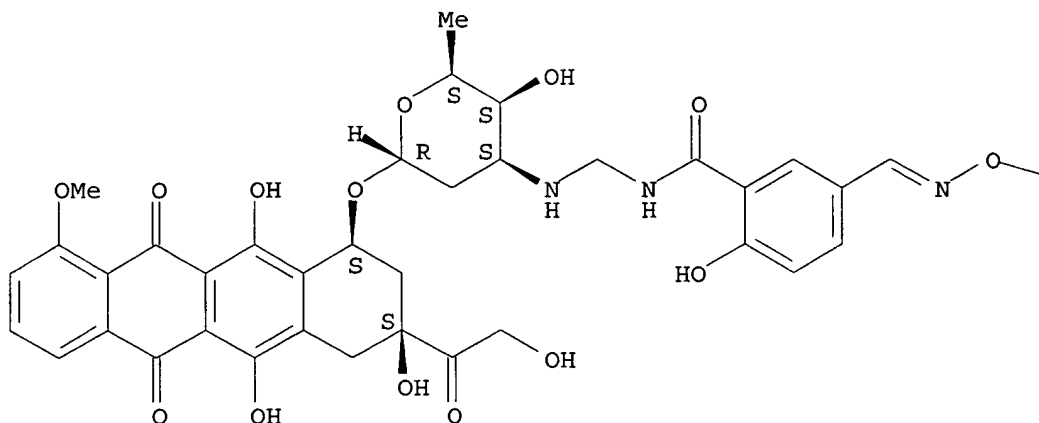
RN 850256-67-6 HCAPLUS

CN Cyclo[L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-N6-[N-[(aminooxy)acetyl]-D- α -aspartyl]-L-lysyl], aldoxime with (8S,10S)-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-10-[[[2,3,6-trideoxy-3-[[[(5-formyl-2-hydroxybenzoyl)amino]methyl]amino]- α -L-lyxo-hexopyranosyl]oxy]-5,12-naphthacenedione (9CI) (CA INDEX NAME)

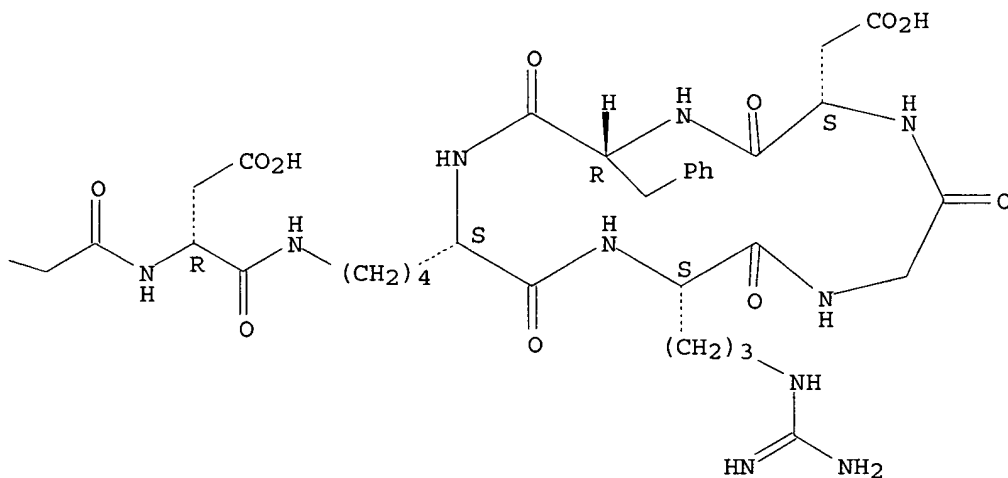
Absolute stereochemistry.

Double bond geometry unknown.

PAGE 1-A



PAGE 1-B



L47 ANSWER 11 OF 43 HCAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2005:218595 HCAPLUS
 DOCUMENT NUMBER: 143:262768
 TITLE: Near-infrared optical imaging of **integrin**
 α v β 3 in human tumor **xenografts**
 AUTHOR(S): Wang, Wei; Ke, Shi; Wu, Qingping; Charnsangavej,
 Chusilp; Gurfinkel, Mikhail; Gelovani, Juri G.;
 Abbruzzese, James L.; Sevic-Muraca, Eva M.; Li, Chun
 CORPORATE SOURCE: The University of Texas M. D. Anderson Cancer Center,
 TX, USA
 SOURCE: Molecular Imaging (2004), 3(4), 343-351
 CODEN: MIOMBP; ISSN: 1535-3508
 PUBLISHER: MIT Press
 DOCUMENT TYPE: Journal

LANGUAGE: English

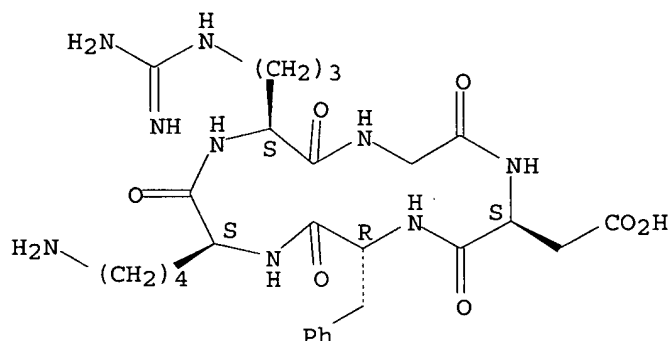
- AB In vivo optical imaging is potentially useful for evaluating the presence of tumor markers that are targets of mol. medicine. Here the authors report the synthesis and characterization of **integrin** $\alpha\beta 3$ -targeted peptide cyclo(Lys-Arg-Gly-Asp-Phe) [c(KRGDf)] labeled with fluorescence dyes with wavelength spanning from the visible/near IR (Cy5.5) to the true near IR (IRDye800) for optical imaging. In vitro, the peptide-dye conjugates bound specifically to tumor cells expressing $\alpha\beta 3$. When administered i.v. into mice at a dose of 6 nmol/mouse, the conjugates accumulated in tumors expressing $\alpha\beta 3$. The tumor-to-background ratios for human KS1767 Kaposi's sarcoma in mice injected with Cy5.5-c(KRGDf) and Cy5.5 were 5.5 and 1.5, resp. Preinjection of c(KRGDf) blocked the uptake of Cy5.5-c(KRGDf) in tumors by 89%. In $\alpha\beta 3$ -pos. M21 and $\alpha\beta 3$ -neg. M21-L human melanoma, fluorescence intensity in the tumor of mice injected with IRDye800-c(KRGDf) was 2.3 and 1.3 times that in normal tissue, resp. Dynamic imaging revealed that Cy5.5-c(KRGDf) was rapidly taken up by KS1767 tumor immediately after bolus injection. The rate of its uptake in the tumor was reduced by preinjection of c(KRGDf) in an interval time-dependent manner. The authors' data suggest that near-IR fluorescence imaging may be applied to the detection of tumors expressing **integrin** $\alpha\beta 3$ and to the assessment of the optimal biol. dose and schedule of targeted therapies.
- CC 9-5 (Biochemical Methods)
- ST near IR fluorescence imaging **integrin** tumor diagnosis;
integrin Cy55 IRDye800 fluorescence imaging tumor
- IT Imaging
(fluorescent; near-IR fluorescence imaging detection of tumors expressing **integrin** $\alpha\beta 3$)
- IT Diagnosis
Fluorometry
Human
Neoplasm
(near-IR fluorescence imaging detection of tumors expressing **integrin** $\alpha\beta 3$)
- IT IR spectroscopy
(near-IR; near-IR fluorescence imaging detection of tumors expressing **integrin** $\alpha\beta 3$)
- IT **Integrins**
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
($\alpha\beta 3$; near-IR fluorescence imaging detection of tumors expressing **integrin** $\alpha\beta 3$)
- IT **161552-03-ODP**, Cy5.5- or IRDye800-labeled 172777-84-3DP, Cy5.5, -labeled c(KRGDf) 211380-08-4DP, IRDye800, -labeled c(KRGDf)
RL: ARG (Analytical reagent use); DGN (Diagnostic use); PRP (Properties); SPN (Synthetic preparation); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(near-IR fluorescence imaging detection of tumors expressing **integrin** $\alpha\beta 3$)
- IT **161552-03-ODP**, Cy5.5- or IRDye800-labeled
RL: ARG (Analytical reagent use); DGN (Diagnostic use); PRP (Properties); SPN (Synthetic preparation); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(near-IR fluorescence imaging detection of tumors expressing **integrin** $\alpha\beta 3$)
- IT **161552-03-ODP**, Cy5.5- or IRDye800-labeled
RL: ARG (Analytical reagent use); DGN (Diagnostic use); PRP (Properties); SPN (Synthetic preparation); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)

(near-IR fluorescence imaging detection of tumors expressing
integrin $\alpha v \beta 3$)

RN 161552-03-0 HCAPLUS

CN Cyclo(L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-L-lysyl) (9CI)
 (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 12 OF 43 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:182691 HCAPLUS

DOCUMENT NUMBER: 142:285150

TITLE: Cyclic peptide and imaging compound compositions and
 uses for targeted imaging and therapy

INVENTOR(S): Li, Chun; Ke, Shi; Wang, Wei

PATENT ASSIGNEE(S): Board of Regents, the University of Texas System, USA

SOURCE: PCT Int. Appl., 92 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005019247	A2	20050303	WO 2004-US26220	20040813
WO 2005019247	A3	20050519		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 2005069494	A1	20050331	US 2004-918009	20040813
PRIORITY APPLN. INFO.:			US 2003-495658P	P 20030815
			US 2004-918009	A 20040813

OTHER SOURCE(S): MARPAT 142:285150

AB The present invention relates to novel cyclic peptides that may be
 conjugated with imaging agents, including novel imaging agents.

Specifically, it includes c(KRGdf) NIR imaging compns. and novel cyclic HWGFTL polypeptides which may be used inter alia in NIR, MRI and nuclear imaging as well as therapy. Addnl., the invention includes novel imaging agents, such as TS-ICG derivs. The invention also relates to methods of making and using such compds. Such uses include both pre-operative and intraoperative detection of tumor cells and treatment monitoring.

- IC ICM C07K007-64
ICS A61K051-08
- CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 8
- IT 1317-61-9D, Iron oxide, peptide-conjugated compds. 1332-37-2D, Iron oxide, peptide-conjugated compds. 7439-96-5D, Manganese, peptide-conjugated compds. 7440-54-2D, Gadolinium, peptide-conjugated compds. 13981-25-4D, Copper 64, peptide-conjugated compds., biological studies 13981-56-1D, Fluorine 18, peptide-conjugated compds., biological studies 14133-76-7D, Technetium 99, peptide-conjugated compds., biological studies 15750-15-9D, Indium 111, peptide-conjugated compds., biological studies 15757-14-9D, Gallium 68, peptide-conjugated compds., biological studies 15757-86-5D, Copper 67, peptide-conjugated compds., biological studies 181786-27-6D, conjugates with IRdye 800 211380-08-4D, IRdye 800, conjugates with a cyclic peptide 847180-59-0 847180-60-3
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(cyclic peptide and imaging compound compns. and uses for targeted imaging and therapy)
- IT 847180-57-8P
RL: DGN (Diagnostic use); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(cyclic peptide and imaging compound compns. and uses for targeted imaging and therapy)
- IT 56-87-1D, L-Lysine, conjugates 70-51-9D, Deferoxamine, Conjugates with MTX and a cyclic peptide 3599-32-4D, conjugates 3599-32-4D, Indocyanine green, peptide conjugates 3599-32-4D, Indocyanine green, sulfonated derivs., peptide conjugates 10043-66-0D, Iodine 131, peptide conjugates labeled with, biological studies 14158-30-6D, Iodine 124, peptide conjugates labeled with, biological studies 14158-31-7D, Iodine 125, peptide conjugates labeled with, biological studies 25322-68-3D, Peg, peptide-conjugates 25513-46-6D, L-Glutamic acid polymer, peptide-conjugates 172777-84-3D, Cy5.5, peptide conjugates 211380-08-4, IRDye 800 211380-08-4D, IRDye800, peptide conjugates 244082-19-7D, conjugates 791772-43-5 847180-39-6D, conjugates 847180-40-9D, conjugates 847180-41-0D, conjugates 847180-42-1D, conjugates 847180-43-2D, conjugates 847180-44-3D, conjugates 847180-45-4D, conjugates 847180-48-7D, conjugates 847180-49-8D, conjugates 847180-50-1D, conjugates 847180-51-2D, conjugates 847180-52-3 847180-52-3D, Conjugates with Deferoxamine 847180-53-4 847180-54-5 847227-29-6
RL: DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cyclic peptide and imaging compound compns. and uses for targeted imaging and therapy)
- IT 181786-27-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(cyclic peptide and imaging compound compns. and uses for targeted imaging and therapy)
- IT 59-05-2D, Methotrexate, peptide-conjugated compds. 7689-03-4D, Camptothecin, peptide-conjugated compds. 10098-91-6D, Yttrium 90, peptide-conjugated compds., biological studies 23214-92-8D, Doxorubicin, peptide-conjugated compds. 33069-62-4D, Paclitaxel,

peptide-conjugated compds.

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cyclic peptide and imaging compound compns. and uses for targeted imaging and therapy)

IT 181786-27-6D, conjugates with IRdye 800

RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(cyclic peptide and imaging compound compns. and uses for targeted imaging and therapy)

IT 847180-57-8P

RL: DGN (Diagnostic use); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(cyclic peptide and imaging compound compns. and uses for targeted imaging and therapy)

IT 847180-50-1D, conjugates 847180-51-2D, conjugates
847180-52-3 847180-52-3D, Conjugates with Deferoxamine
847180-53-4 847180-54-5 847227-29-6

RL: DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cyclic peptide and imaging compound compns. and uses for targeted imaging and therapy)

IT 181786-27-6

RL: RCT (Reactant); RACT (Reactant or reagent)
(cyclic peptide and imaging compound compns. and uses for targeted imaging and therapy)

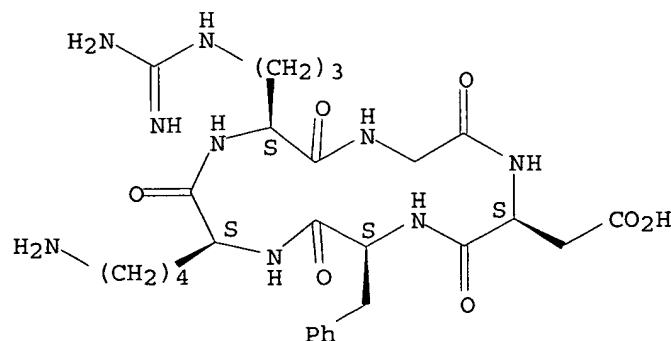
IT 181786-27-6D, conjugates with IRdye 800

RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(cyclic peptide and imaging compound compns. and uses for targeted imaging and therapy)

RN 181786-27-6 HCAPLUS

CN Cyclo(L-arginylglycyl-L- α -aspartyl-L-phenylalanyl-L-lysyl) (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



IT 847180-57-8P

RL: DGN (Diagnostic use); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(cyclic peptide and imaging compound compns. and uses for targeted imaging and therapy)

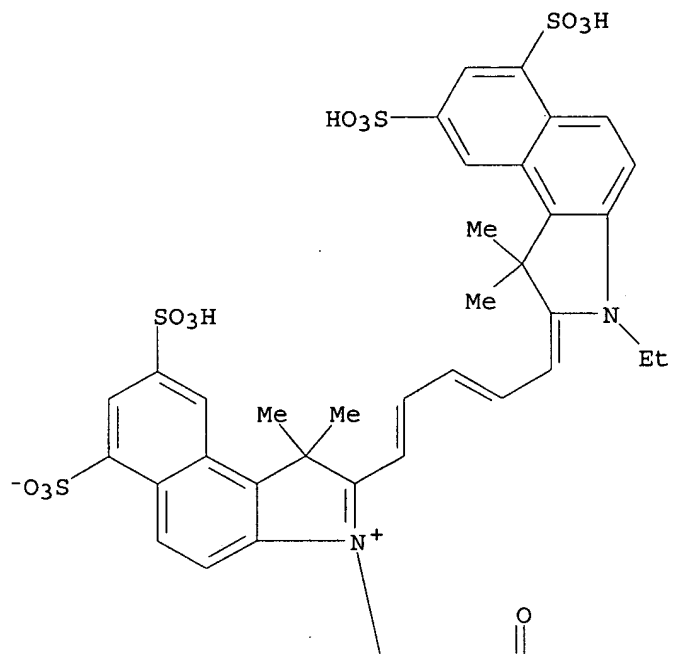
RN 847180-57-8 HCAPLUS

CN Cyclo[L-arginylglycyl-L- α -aspartyl-L-phenylalanyl-N6-[6-[2-[5-(3-ethyl-1,3-dihydro-1,1-dimethyl-6,8-disulfo-2H-benz[e]indol-2-ylidene)-1,3-pentadienyl]-1,1-dimethyl-6,8-disulfo-1H-benz[e]indol-1-oxohexyl]-L-lysyl], inner salt (9CI) (CA INDEX NAME)

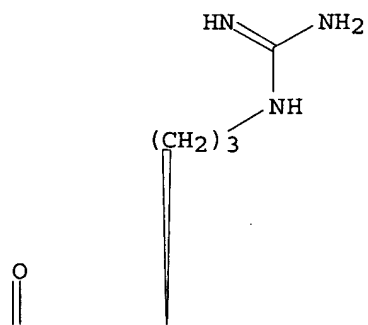
Absolute stereochemistry.

Double bond geometry unknown.

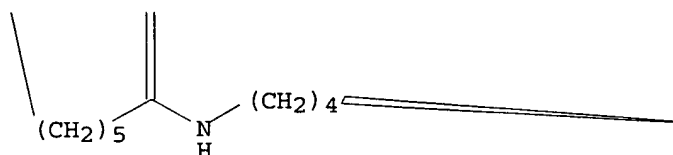
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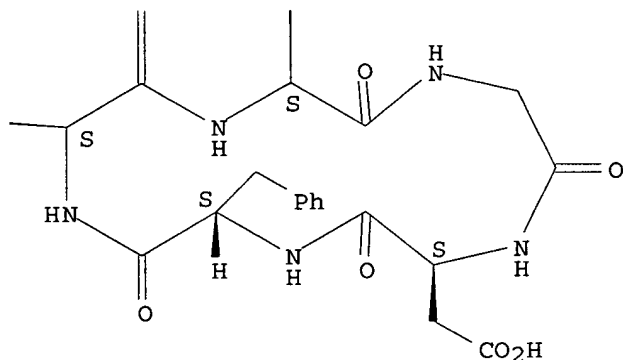
PAGE 1-B



PAGE 2-A



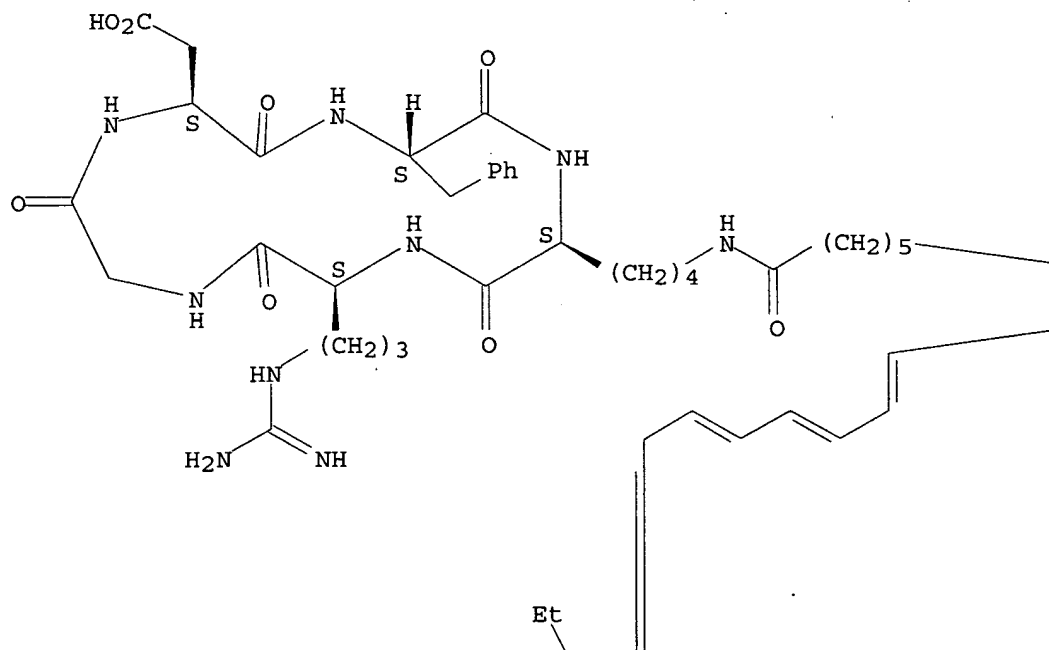
PAGE 2-B



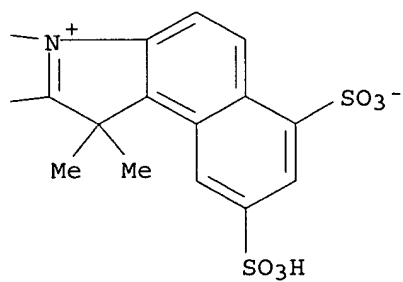
IT 847180-50-1D, conjugates 847180-51-2D, conjugates
 847180-52-3 847180-52-3D, Conjugates with Deferoxamine
 847180-53-4 847180-54-5 847227-29-6
 RL: DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study);
 USES (Uses)
 (cyclic peptide and imaging compound compns. and uses for targeted
 imaging and therapy)
 RN 847180-50-1 HCAPLUS
 CN Cyclo[L-arginylglycyl-L- α -aspartyl-L-phenylalanyl-N6-[6-[2-[7-(3-
 ethyl-1,3-dihydro-1,1-dimethyl-6,8-disulfo-2H-benz[e]indol-2-ylidene)-
 1,3,5-heptatrienyl]-1,1-dimethyl-6,8-disulfo-1H-benz[e]indolio]-1-
 oxohexyl]-L-lysyl], inner salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry unknown.

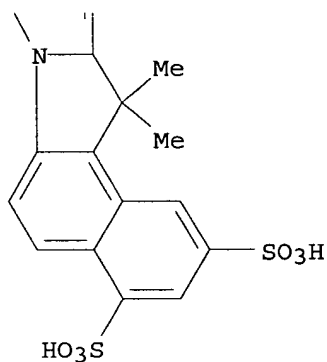
PAGE 1-A



PAGE 1-B



PAGE 2-A

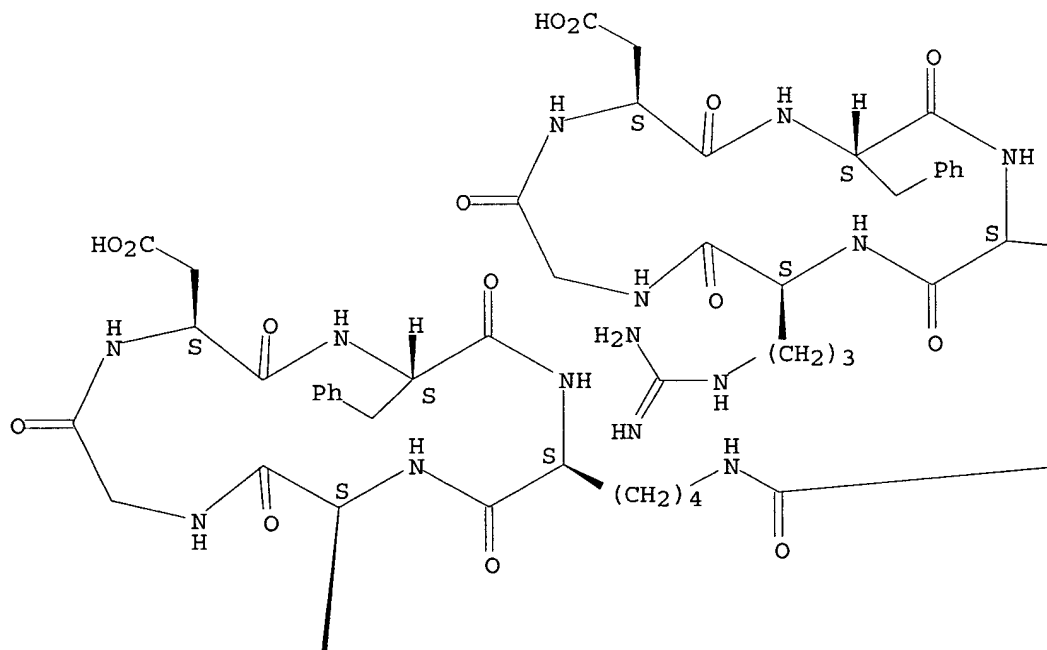


RN 847180-51-2 HCAPLUS

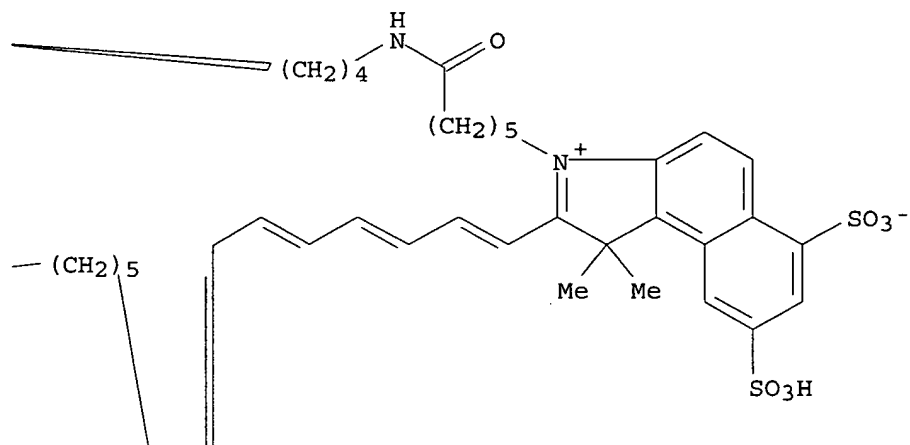
CN Cyclo[L-arginylglycyl-L-α-aspartyl-L-phenylalanyl-N6-[6-[2-[7-[3-(5-carboxypentyl)-1,3-dihydro-1,1-dimethyl-6,8-disulfo-2H-benz[e]indol-2-ylidene]-1,3,5-heptatrienyl]-1,1-dimethyl-6,8-disulfo-1H-benz[e]indolio]-1-oxohexyl]-L-lysyl], inner salt, (5→5')-amide with cyclo(L-arginylglycyl-L-α-aspartyl-L-phenylalanyl-L-lysyl) (9CI)
(CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

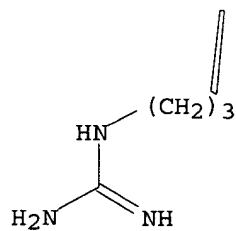
PAGE 1-A



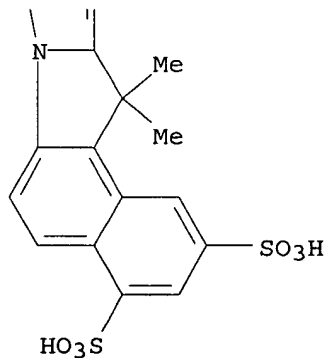
PAGE 1-B



PAGE 2-A



PAGE 2-B

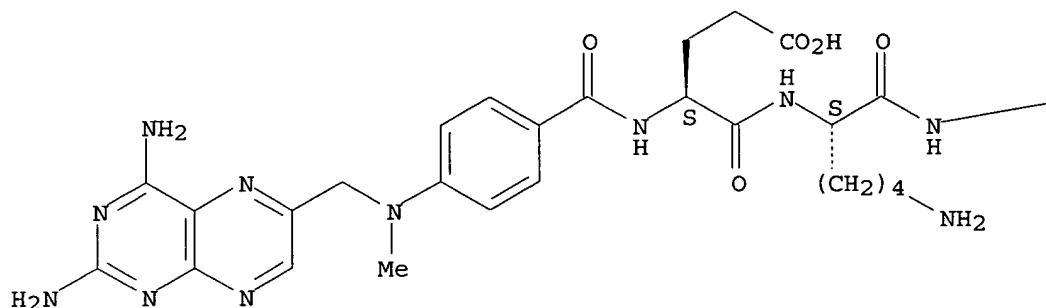


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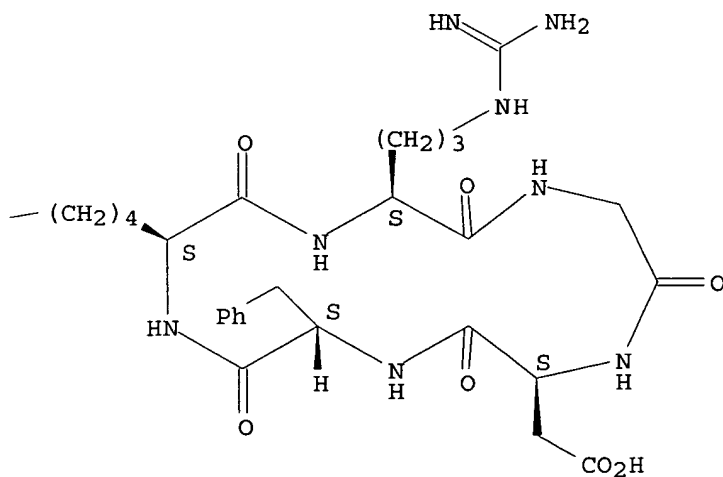
CN Cyclo[L-arginylglycyl-L- α -aspartyl-L-phenylalanyl-N6-[N-[4-[[[2,4-diamino-6-pteridiny]methyl]methylamino]benzoyl]-L- α -glutamyl-L-lysyl]-L-lysyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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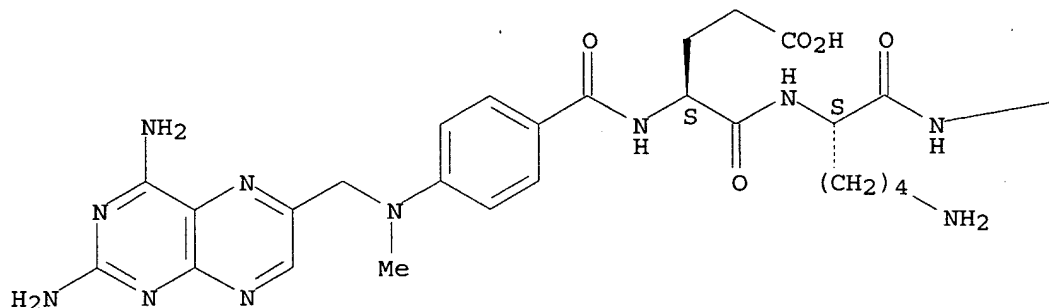


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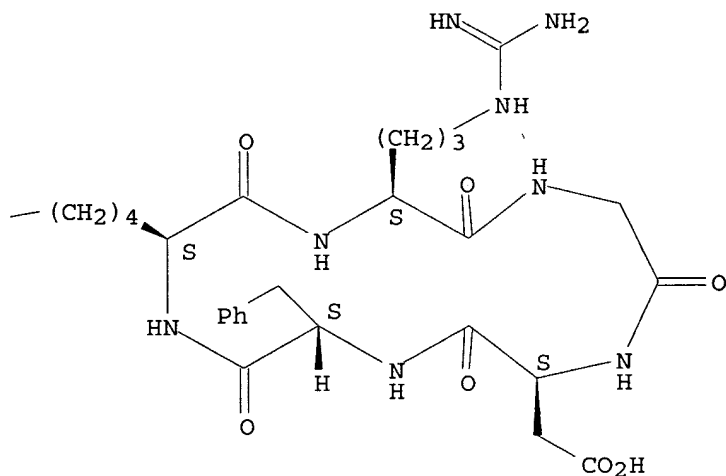
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Absolute stereochemistry.

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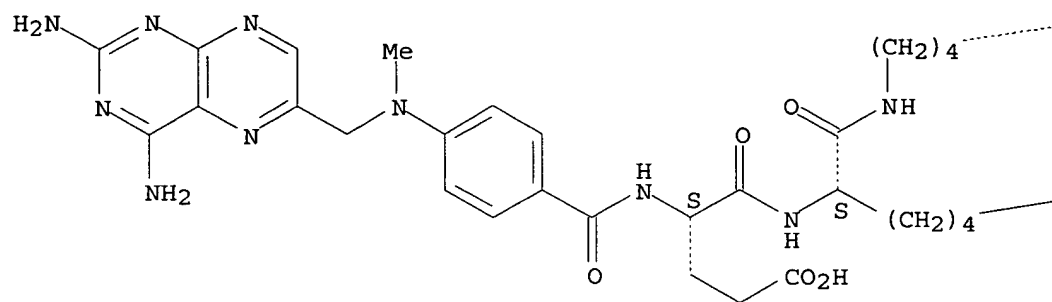


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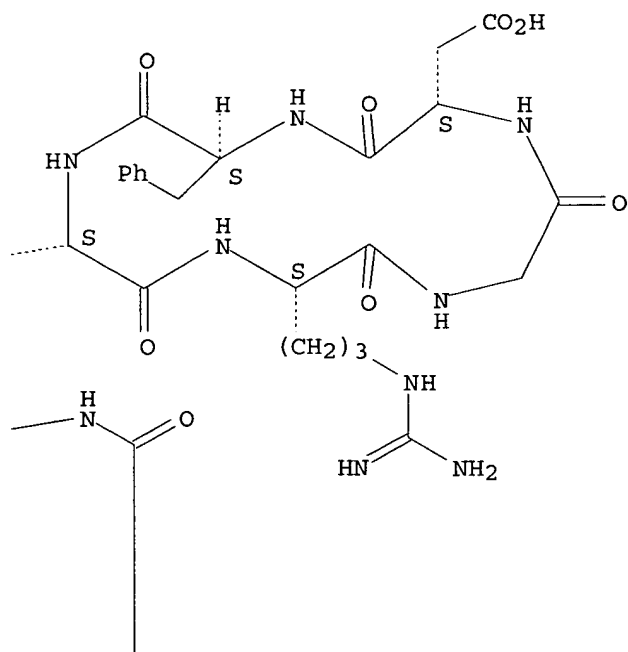
CN Cyclo[L-arginylglycyl-L- α -aspartyl-L-phenylalanyl-N6-[N-[4-[[[2,4-diamino-6-pteridiny]methyl]methylamino]benzoyl]-L- α -glutamyl-N6-[6-[2-[7-[3-(5-carboxypentyl)-1,3-dihydro-1,1-dimethyl-2H-benz[e]indol-2-ylidene]-1,3,5-heptatrienyl]-1,1-dimethyl-1H-benz[e]indolio]-1-oxohexyl]-L-lysyl]-L-lysyl], inner salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

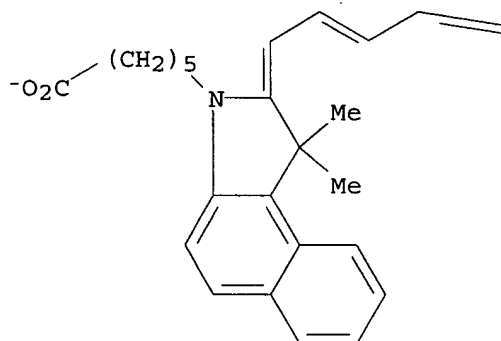
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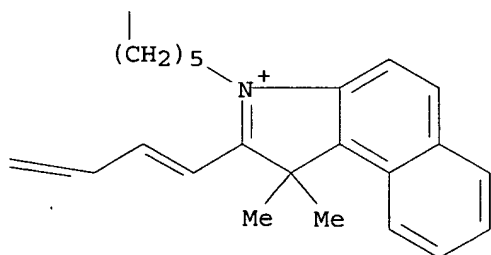
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PAGE 2-A



PAGE 2-B

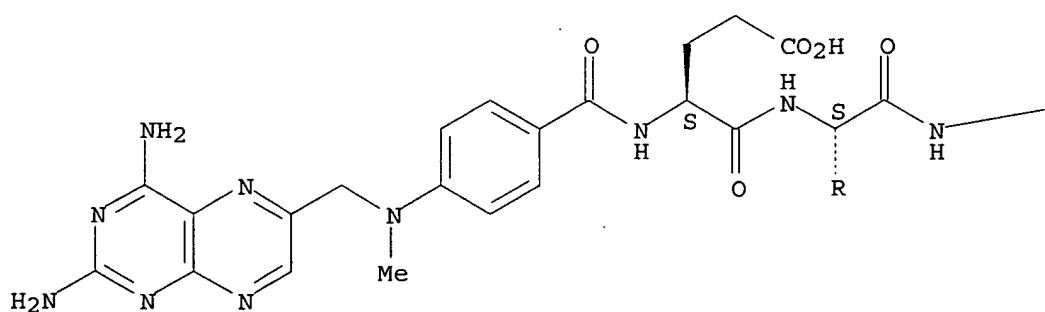


RN 847180-54-5 HCAPLUS

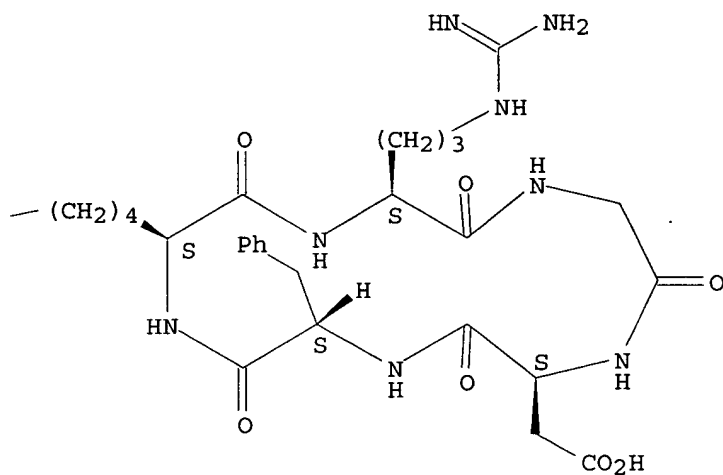
CN Cyclo[L-arginylglycyl-L-α-aspartyl-L-phenylalanyl-N6-[N-[4-[[[(2,4-diamino-6-pteridiny]methyl)methylamino]benzoyl]-L-α-glutamyl-N6-[N-[2-[[2-[bis(carboxymethyl)amino]ethyl](carboxymethyl)amino]ethyl]-N-(carboxymethyl)glycyl]-L-lysyl]-L-lysyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.

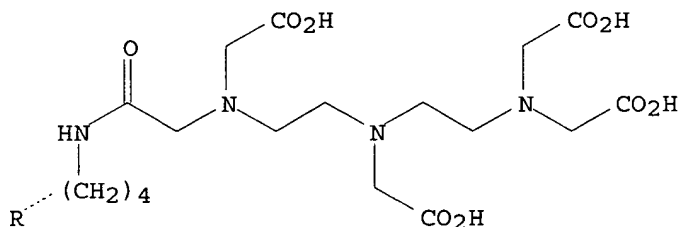
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PAGE 1-B

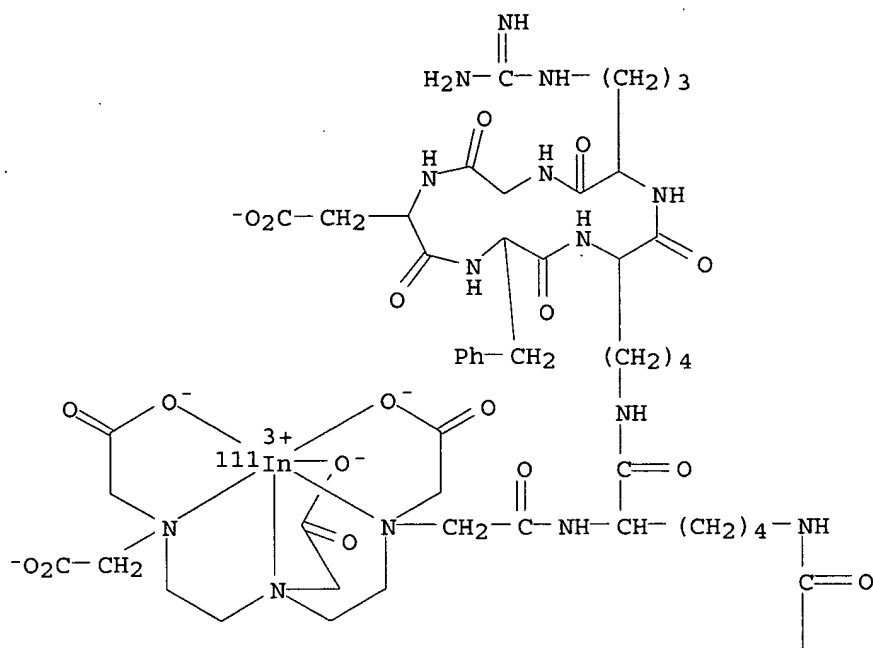


PAGE 2-A

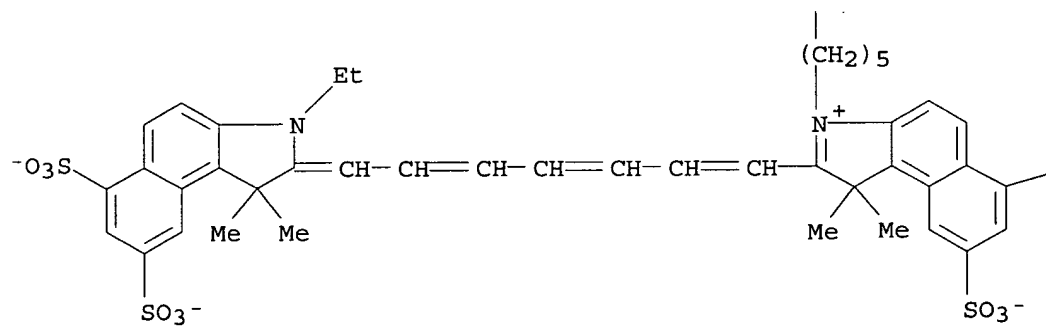


RN 847227-29-6 HCAPLUS
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PAGE 1-A



PAGE 2-A



● 5 H^+

PAGE 2-B

— SO_3^-

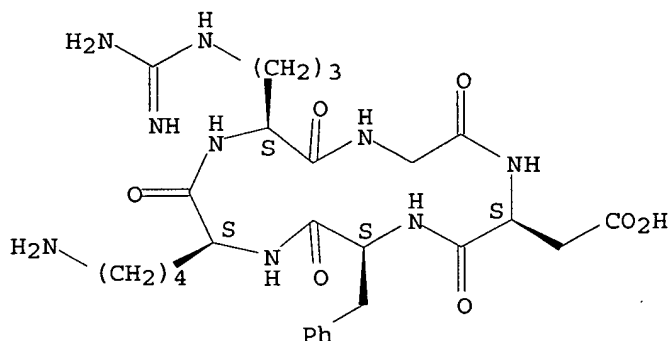
IT 181786-27-6

RL: RCT (Reactant); RACT (Reactant or reagent)
(cyclic peptide and imaging compound compns. and uses for targeted
imaging and therapy)

RN 181786-27-6 HCAPLUS

CN Cyclo(L-arginylglycyl-L- α -aspartyl-L-phenylalanyl-L-lysyl) (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



L47 ANSWER 13 OF 43 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:121193 HCAPLUS

DOCUMENT NUMBER: 142:214836

TITLE: Biomarkers of cyclin-dependent kinase modulation in
cancer therapy

INVENTOR(S): Li, Martha; Rupnow, Brent A.; Webster, Kevin R.;
Jackson, Donald G.; Wong, Tai W.

PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA

SOURCE: PCT Int. Appl., 141 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005012875	A2	20050210	WO 2004-US24424	20040729
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004262369	A1	20050210	AU 2004-262369	20040729
CA 2533803	AA	20050210	CA 2004-2533803	20040729
EP 1656542	A2	20060517	EP 2004-779471	20040729
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
PRIORITY APPLN. INFO.:			US 2003-490890P	P 20030729

WO 2004-US24424

W 20040729

AB Biomarkers having expression patterns that correlate with a response of cells to treatment with one or more cdk modulating agents, and uses thereof. Transcription profiling was used to identify the biomarkers. Specifically, transcription profiling of the effect of a certain cdk2 inhibitor (BMS 387032 0.5 L-tartaric acid salt) on peripheral blood mononuclear cells was first performed. Gene chips were used to quantitate the levels of gene expression on a large-scale with Affymetrix human gene chips HG-U95A, B, and C. Next, profiling of a cdk2 inhibitor-treated tumor cell line A28780 at multiple doses and time points was performed to establish a correlation of tumor site response with peripheral blood biomarkers. In order to establish the mol. target-specificity of the potential biomarkers, tumor cell line A2780 treated with anti-cdk2 oligonucleotides was also profiles. Overlapping gene expression changes were selected for further evaluation in human ovarian carcinoma **xenograft** A2780 that were treated with the cdk2 inhibitor. The selected biomarkers were subjected to real-time PCR anal. in order to verify the observed changes from the gene chip anal. The biomarker comprising GenBank accession number W28729 was discovered to have the most consistent and robust regulation in response to cdk inhibition. Provided are methods for testing or predicting whether a mammal will respond therapeutically to a method of treating cancer that comprises administering an agent that modulates cdk activity.

IC ICM G01N

CC 9-3 (Biochemical Methods)

Section cross-reference(s): 3, 63

IT **Ribosomal proteins**

RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(S5; biomarkers of cyclin-dependent kinase modulation in cancer therapy)

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RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(amino acid sequence; biomarkers of cyclin-dependent kinase modulation in cancer therapy)

IT **841324-08-1**

RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(amino acid sequence; biomarkers of cyclin-dependent kinase modulation in cancer therapy)

IT **841324-08-1**

RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(amino acid sequence; biomarkers of cyclin-dependent kinase modulation in cancer therapy)

RN 841324-08-1 HCAPLUS

CN Cyclin-dependent kinase modulator-regulated protein (human clone WO2005012875-SEQID-147) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L47 ANSWER 14 OF 43 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:1130047 HCAPLUS

DOCUMENT NUMBER: 142:435638

TITLE: In vivo study of the effect of RGD treatment on bone ongrowth on press-fit titanium alloy implants

AUTHOR(S): Elmengaard, Brian; Bechtold, Joan E.; Soballe, Kjeld

CORPORATE SOURCE: Orthopaedic Research Laboratory, Department of Orthopaedic Surgery, AKH, Aarhus University Hospital, Aarhus C, DK-8000, Den.

SOURCE: Biomaterials (2005), 26(17), 3521-3526

CODEN: BIMADU; ISSN: 0142-9612

PUBLISHER: Elsevier Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Early bone ongrowth is known to increase primary implant fixation and reduce the risk of early implant failure. Arg-Gly-Asp (RGD) peptide has been identified as playing a key role in osteoblast adhesion and proliferation on various surfaces. The aim for this study is to evaluate the effect of RGD peptide coating on the bony fixation of orthopedic implants, to justify its further evaluation in clin. applications. Sixteen unloaded cylindrical plasma sprayed Ti6Al4 V implants coated with cyclic RGD peptide were inserted as press-fit in the proximal

tibia of 8 mongrel dogs for 4 wk. Uncoated control implants were inserted in the contralateral tibia. Results were evaluated by histomorphometry and mech. push-out test. A significant two-fold increase was observed in bone ongrowth for RGD-coated implants. Also, fibrous tissue ongrowth was significantly reduced for RGD-coated implants. Bone volume was significantly increased in a 0-100 μ m zone around the implant. The increased bony anchorage resulted in moderate increases in mech. fixation as apparent shear stiffness was significantly higher for RGD-coated implants. Increases in median ultimate shear strength and energy to failure were also observed. This study demonstrates that cyclic RGD coating increases early bony fixation of unloaded press-fit titanium implants.

CC 63-6 (Pharmaceuticals)

IT 12743-70-3, Ti6al4v 190072-28-7

RL: BSU (Biological study, unclassified); DEV (Device component use); PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(RGD peptide treatment effect on bone ongrowth on press-fit titanium alloy implants)

IT 190072-28-7

RL: BSU (Biological study, unclassified); DEV (Device component use); PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(RGD peptide treatment effect on bone ongrowth on press-fit titanium alloy implants)

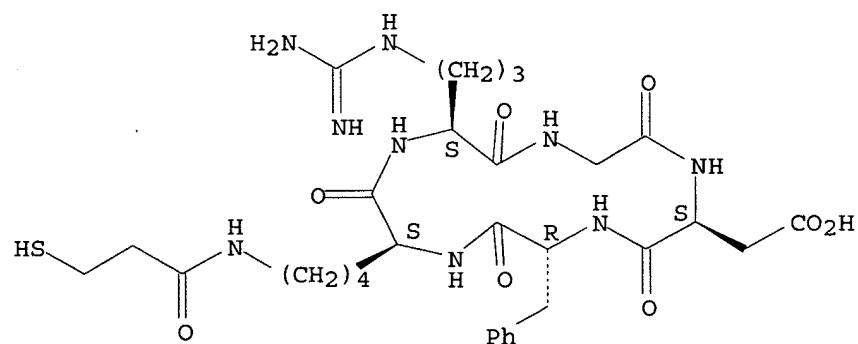
IT 190072-28-7

RL: BSU (Biological study, unclassified); DEV (Device component use); PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(RGD peptide treatment effect on bone ongrowth on press-fit titanium alloy implants)

RN 190072-28-7 HCAPLUS

CN Cyclo[L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-N6-(3-mercapto-1-oxopropyl)-L-lysyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 15 OF 43 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:1118616 HCAPLUS

DOCUMENT NUMBER: 142:225477

TITLE: Bioorganic chemistry: cRGD-functionalized polymer micelles for targeted doxorubicin delivery

AUTHOR(S): Nasongkla, Norased; Shuai, Xintao; Ai, Hua; Weinberg, Brent D.; Pink, John; Boothman, David A.; Gao, Jinming

CORPORATE SOURCE: Department of Biomedical Engineering, Case Western Reserve University, Cleveland, OH, 44106, USA

SOURCE: Angewandte Chemie, International Edition (2004), 43(46), 6323-6327
CODEN: ACIEF5; ISSN: 1433-7851

PUBLISHER: - Wiley-VCH Verlag GmbH & Co. KGaA

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Targeting micelles: Cyclic pentapeptide cRGDFK (red triangles), which targets **integrin** $\alpha\beta_3$, was conjugated to the outer shell of **doxorubicin**-loaded (red hexagons) polymeric micelles by using a post-micelle modification method. The modified micelles significantly enhanced their internalization (up to 30-fold) by receptor-mediated endocytosis in tumor endothelial cells overexpressing the $\alpha\beta_3$ receptor.

CC 63-5 (Pharmaceuticals)

ST polycaprolactone PEG **doxorubicin** RGD peptide micelle

IT Endothelium
Micelles
Particle size
(cRGD-functionalized polymer micelles for targeted **doxorubicin** delivery)

IT RGD peptides
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cRGD-functionalized polymer micelles for targeted **doxorubicin** delivery)

IT Polyoxyalkylenes, biological studies
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polyester-; cRGD-functionalized polymer micelles for targeted **doxorubicin** delivery)

IT Polyesters, biological studies
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polyoxyalkylene-; cRGD-functionalized polymer micelles for targeted **doxorubicin** delivery)

IT **Integrins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
($\alpha\beta_3$; cRGD-functionalized polymer micelles for targeted **doxorubicin** delivery)

IT 841255-52-5P
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(cRGD-functionalized polymer micelles for targeted **doxorubicin** delivery)

IT **841255-57-0P**
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(cRGD-functionalized polymer micelles for targeted **doxorubicin** delivery)

IT **161552-03-0**
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cRGD-functionalized polymer micelles for targeted **doxorubicin** delivery)

IT 23214-92-8, **Doxorubicin** 29022-11-5D, Fmoc-Gly-OH, peptide-resin conjugate 76931-93-6 86123-10-6D, Fmoc-D-Phe-OH, peptide-resin conjugate 144120-53-6D, resin conjugate 150629-67-7D, Fmoc-Lys(Dde)-OH, peptide-resin conjugate 154445-77-9D,

Fmoc-Arg(Pbf)-OH, peptide-resin conjugate 478242-36-3, NovaSyn TGT
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (cRGD-functionalized polymer micelles for targeted **doxorubicin** delivery)

IT 393781-65-2P 478242-36-3DP, NovaSyn TGT, derivs.
 841255-53-6DP, resin conjugate 841255-54-7DP, resin conjugate
 841255-55-8DP, resin conjugate 841255-56-9DP, resin conjugate
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (cRGD-functionalized polymer micelles for targeted **doxorubicin** delivery)

IT 841255-57-0P
 RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (cRGD-functionalized polymer micelles for targeted **doxorubicin** delivery)

IT 161552-03-0
 RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (cRGD-functionalized polymer micelles for targeted **doxorubicin** delivery)

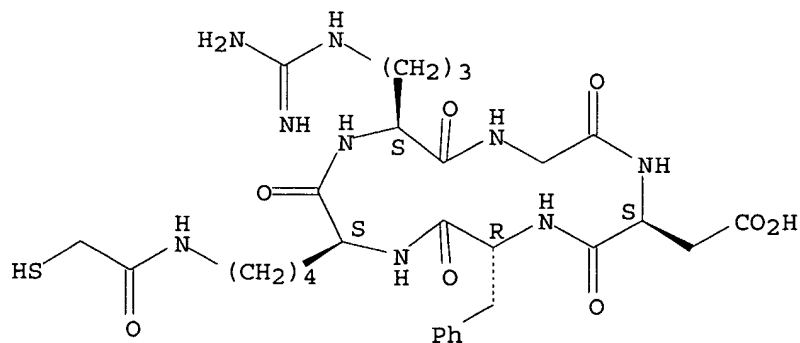
IT 393781-65-2P 841255-54-7DP, resin conjugate
 841255-55-8DP, resin conjugate 841255-56-9DP, resin conjugate
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (cRGD-functionalized polymer micelles for targeted **doxorubicin** delivery)

IT 841255-57-0P
 RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (cRGD-functionalized polymer micelles for targeted **doxorubicin** delivery)

RN 841255-57-0 HCAPLUS

CN Cyclo[L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-N6-(mercaptoacetyl)-L-lysyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.

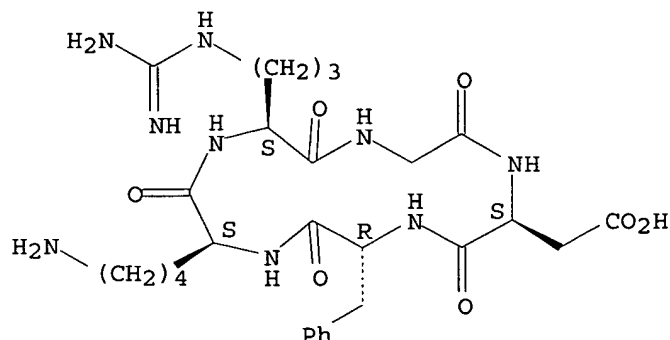


IT 161552-03-0
 RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (cRGD-functionalized polymer micelles for targeted **doxorubicin** delivery)

RN 161552-03-0 HCAPLUS

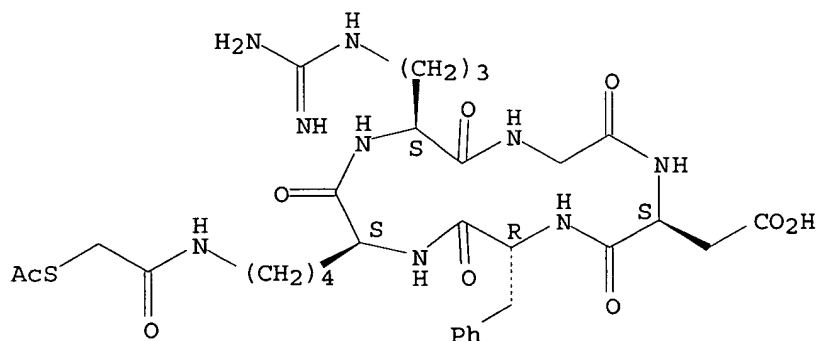
CN Cyclo(L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-L-lysyl) (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



IT 393781-65-2P 841255-54-7DP, resin conjugate
841255-55-8DP, resin conjugate 841255-56-9DP, resin
conjugate
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(cRGD-functionalized polymer micelles for targeted **doxorubicin**
delivery)
RN 393781-65-2 HCAPLUS
CN Cyclo[L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-N6-
[(acetylthio)acetyl]-L-lysyl] (9CI) (CA INDEX NAME)

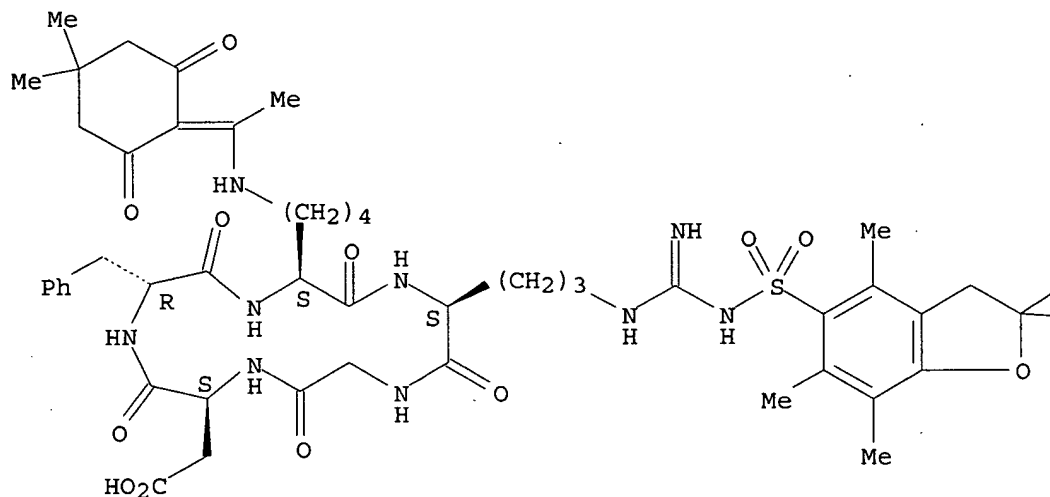
Absolute stereochemistry.



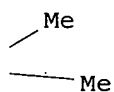
RN 841255-54-7 HCAPLUS
CN Cyclo[L- α -aspartyl-D-phenylalanyl-N6-[1-(4,4-dimethyl-2,6-
dioxocyclohexylidene)ethyl]-L-lysyl-N5-[[[(2,3-dihydro-2,2,4,6,7-
pentamethyl-5-benzofuranyl)sulfonyl]amino]iminomethyl]-L-ornithylglycyl]
(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



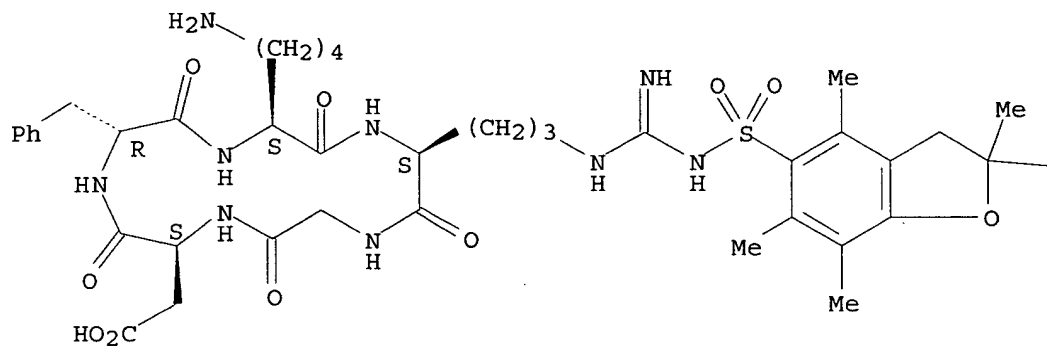
PAGE 1-B



RN 841255-55-8 HCAPLUS
 CN Cyclo[L- α -aspartyl-D-phenylalanyl-L-lysyl-N5-[[[(2,3-dihydro-2,2,4,6,7-pentamethyl-5-benzofuranyl)sulfonyl]amino]iminomethyl]-L-ornithylglycyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

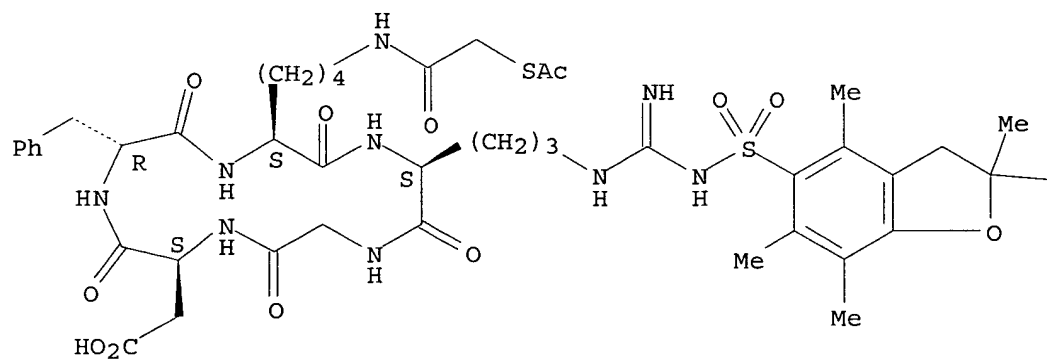
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RN 841255-56-9 HCAPLUS

CN Cyclo[L- α -aspartyl-D-phenylalanyl-N6-[(acetylthio)acetyl]-L-lysyl-N5-
[[[(2,3-dihydro-2,2,4,6,7-pentamethyl-5-benzofuranyl)sulfonyl]amino]iminom
ethyl]-L-ornithylglycyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

— Me

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 16 OF 43 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:1071204 HCAPLUS

DOCUMENT NUMBER: 142:198295

TITLE: New strategy for the synthesis of 3',5'-bi-functionalized oligonucleotide conjugates through sequential formation of chemoselective **oxime** bonds

AUTHOR(S): Edupuganti, Om Prakash; Singh, Yashveer; Defrancq, Eric; Dumy, Pascal

CORPORATE SOURCE: LEDSS, UMR CNRS 5616, ICMG FR2607, Universite Joseph Fourier, Grenoble, 38041/9, Fr.

SOURCE: Chemistry--A European Journal (2004), 10(23), 5988-5995

CODEN: CEUJED; ISSN: 0947-6539

PUBLISHER: Wiley-VCH Verlag GmbH & Co. KGaA

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 142:198295

AB A convenient strategy for the synthesis of bi-functionalized oligonucleotide conjugates bearing two different reporters at the 3' and 5' ends of the oligonucleotide is presented. The method involves the preparation of oligonucleotides bearing an aldehyde and/or amino-oxy functionality at each end, followed by reaction to form **oxime** bonds with appropriately functionalized reporters. The conjugation reactions are carried out under mild aqueous conditions with good reaction yield.

CC 33-10 (Carbohydrates)

Section cross-reference(s): 34

ST PNA peptide nucleic acid prepn DNA duplex **oxime** bond; oligodeoxyribonucleotide DNA duplex peptide prepn chemoselective **oxime** bond

IT DNA

RL: SPN (Synthetic preparation); PREP (Preparation) (double-stranded; synthesis of 3',5'-bi-functionalized oligonucleotide conjugates through sequential formation of chemoselective **oxime** bonds)

IT Oligodeoxyribonucleotides

RL: SPN (Synthetic preparation); PREP (Preparation) (duplexes; synthesis of 3',5'-bi-functionalized oligonucleotide conjugates through sequential formation of chemoselective **oxime** bonds)

IT Peptide nucleic acids

RL: SPN (Synthetic preparation); PREP (Preparation) (synthesis of 3',5'-bi-functionalized oligonucleotide conjugates through sequential formation of chemoselective **oxime** bonds)

IT 836691-88-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(bn sxsynthesis of 3',5'-bi-functionalized oligonucleotide conjugates through sequential formation of chemoselective **oxime** bonds)

IT 106-69-4, 1,2,6-Hexanetriol 280578-02-1 **343312-27-6**

343312-28-7 388633-51-0 388633-56-5 388633-58-7

627904-36-3D, CPG polymer support

RL: RCT (Reactant); RACT (Reactant or reagent)

(synthesis of 3',5'-bi-functionalized oligonucleotide conjugates through sequential formation of chemoselective **oxime** bonds)

IT 148254-22-2P 162848-39-7P 836691-89-5P 837431-08-0P 837431-09-1P

837431-10-4P 837431-13-7P 837431-14-8P 837431-15-9P 837431-17-1P

837431-18-2P 837431-20-6P 837431-21-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(synthesis of 3',5'-bi-functionalized oligonucleotide conjugates through sequential formation of chemoselective **oxime** bonds)

IT 835930-28-4P 836691-90-8P 837431-11-5P 837431-12-6P 837431-16-0P

837431-19-3P 837431-22-8P 837431-23-9P 837431-24-0P

RL: SPN (Synthetic preparation); PREP (Preparation)

(synthesis of 3',5'-bi-functionalized oligonucleotide conjugates through sequential formation of chemoselective **oxime** bonds)

IT **343312-27-6** **343312-28-7**

RL: RCT (Reactant); RACT (Reactant or reagent)

(synthesis of 3',5'-bi-functionalized oligonucleotide conjugates through sequential formation of chemoselective **oxime** bonds)

IT **343312-27-6** **343312-28-7**

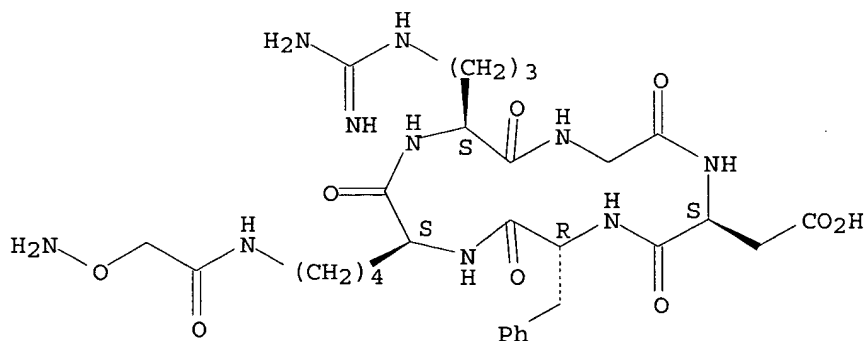
RL: RCT (Reactant); RACT (Reactant or reagent)

(synthesis of 3',5'-bi-functionalized oligonucleotide conjugates through sequential formation of chemoselective **oxime** bonds)

RN 343312-27-6 HCAPLUS

CN Cyclo[L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-N6-(aminooxy)acetyl]-L-lysyl] (9CI) (CA INDEX NAME)

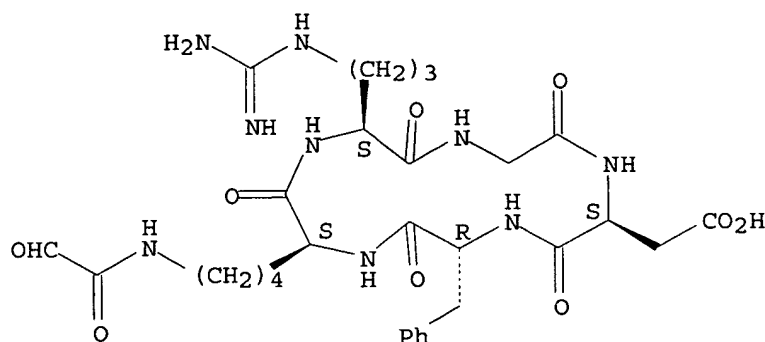
Absolute stereochemistry.



RN 343312-28-7 HCAPLUS

CN Cyclo[L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-N6-(oxoacetyl)-L-lysyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 58 THERE ARE 58 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 17 OF 43 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:1041964 HCAPLUS

DOCUMENT NUMBER: 142:360686

TITLE: Mediating specific cell adhesion to low-adhesive diblock copolymers by instant modification with cyclic RGD peptides

AUTHOR(S): Lieb, E.; Hacker, M.; Tessmar, J.; Kunz-Schughart, L. A.; Fiedler, J.; Dahmen, C.; Hersel, U.; Kessler, H.; Schulz, M. B.; Goepferich, A.

CORPORATE SOURCE: Department of Pharmaceutical Technology, University of Regensburg, Regensburg, 93040, Germany

SOURCE: Biomaterials (2005), 26(15), 2333-2341

CODEN: BIMADU; ISSN: 0142-9612

PUBLISHER: Elsevier Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB One promising strategy to control the interactions between biomaterial surfaces and attaching cells involves the covalent **grafting** of adhesion peptides to polymers on which protein adsorption, which mediates unspecific cell adhesion, is essentially suppressed. This study demonstrates a surface modification concept for the covalent anchoring of RGD peptides to reactive diblock copolymers based on monoamine poly(ethylene glycol)-block-poly(δ , λ -lactic acid) (H2N-PEG-PLA). Films of both the amine-reactive (ST-NH-PEG2PLA20) and the thiol-reactive derivative (MP-NH-PEG2PLA40) were modified with cyclic α v β 3/ α v β 5 **integrin** subtype specific RGD peptides simply by incubation of the films with buffered solns. of the peptides. Human osteoblasts known to express these **integrins** were used to determine cell-polymer interactions. The adhesion expts. revealed significantly increased cell nos. and cell spreading on the RGD-modified surfaces mediated by RGD-**integrin**-interactions.

CC 63-7 (Pharmaceuticals)

IT 161552-03-0 663934-76-7 663949-59-5 848952-31-8

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(mediating specific cell adhesion to low-adhesive diblock copolymers by instant modification with cyclic RGD peptides)

IT 161552-03-0

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(mediating specific cell adhesion to low-adhesive diblock copolymers by instant modification with cyclic RGD peptides)

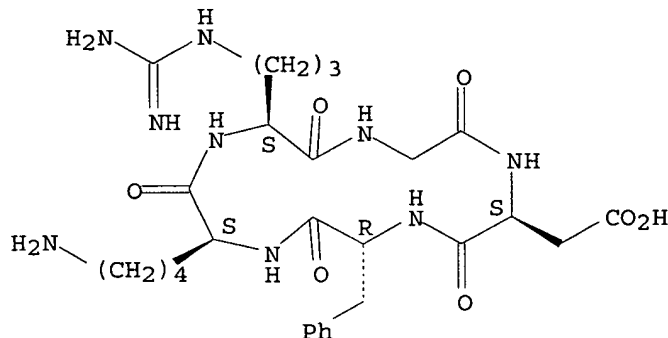
IT 161552-03-0

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mediating specific cell adhesion to low-adhesive diblock copolymers by instant modification with cyclic RGD peptides)

RN 161552-03-0 HCAPLUS

CN Cyclo(L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-L-lysyl) (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 18 OF 43 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:974928 HCAPLUS

DOCUMENT NUMBER: 143:22229

TITLE: Pegylated Arg-Gly-Asp peptide: ^{64}Cu labeling and PET imaging of brain tumor $\alpha\text{v}\beta 3$ -**integrin** expression

AUTHOR(S): Chen, Xiaoyuan; Hou, Yingping; Tohme, Michel; Park, Ryan; Khankaldyyan, Vazgen; Gonzales-Gomez, Ignacio; Bading, James R.; Laug, Walter E.; Conti, Peter S.
CORPORATE SOURCE: PET Imaging Science Center, Keck School of Medicine, University of Southern California, Los Angeles, CA, USA

SOURCE: Journal of Nuclear Medicine (2004), 45(10), 1776-1783
CODEN: JNMEAQ; ISSN: 0161-5505

PUBLISHER: Society of Nuclear Medicine

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The αv - **integrins**, cell adhesion mols. that are highly expressed on activated endothelial cells and tumor cells but not on dormant endothelial cells or normal cells, present an attractive target for tumor imaging and therapy. We previously coupled a cyclic Arg-Gly-Asp (RGD) peptide, c(RGDyK), with 1,4,7,10-tetraazacyclododecane-N,N',N'',N'''-tetraacetic acid (DOTA) and labeled the RGD-DOTA conjugate with ^{64}Cu (half-life, 12.8 h; 19% β^+) for solid tumor targeting, with high tumor-to-background contrast. The rapid tumor washout rate and persistent liver and kidney retention of this tracer prompted us to optimize the tracer for improved pharmacokinetic behavior. In this study, we introduced a polyethylene glycol (PEG; mol. weight, 3,400) moiety between DOTA and RGD and evaluated the ^{64}Cu -DOTA-PEG-RGD tracer for microPET imaging in brain tumor models. Methods: DOTA was activated in situ and conjugated with RGD-PEG-NH₂ under slightly basic conditions. $\alpha\text{v}\beta 3$ - **Integrin**-binding affinity was evaluated with a

solid-phase receptor-binding assay in the presence of ^{125}I -echistatin. Female nude mice bearing s.c. U87MG glioblastoma **xenografts** were administered ^{64}Cu -DOTA-PEG-RGD, and the biodistributions of the radiotracer were evaluated from 30 min to 4 h after injection. MicroPET (20 min of static imaging at 1 h after injection) and then quant. autoradiog. were used for tumor visualization and quantification. The same tracer was also applied to an orthotopic U87MG model for tumor detection. Results: The radiotracer was synthesized with a high specific activity (14,800-29,600 GBq/mmol [400-800 Ci/mmol]). The c(RGDyK)-PEG-DOTA ligand showed intermediate binding affinity for $\alpha\text{v}\beta 3$ - **integrin** (50% inhibitory concentration, 67.5 ± 7.8 nmol/L [mean \pm SD]). The pegylated RGD peptide demonstrated rapid blood clearance (0.57 ± 0.15 percentage injected dose [%ID]/g [mean \pm SD] at 30 min after injection and 0.03 ± 0.02 %ID/g at 4 h after injection). Activity accumulation in the tumor was rapid and high at early time points (2.74 ± 0.45 %ID/g at 30 min after injection), and some activity washout was seen over time (1.62 ± 0.18 %ID/g at 4 h after injection). Compared with ^{64}Cu -DOTA-RGD, this tracer showed improved in vivo kinetics, with significantly reduced liver uptake (0.99 ± 0.08 %ID/g vs. 1.73 ± 0.39 %ID/g at 30 min after injection and 0.58 ± 0.07 %ID/g vs. 2.57 ± 0.49 %ID/g at 4 h after injection). The pegylated RGD peptide showed higher renal accumulation at early time points (3.51 ± 0.24 %ID/g vs. 2.18 ± 0.23 %ID/g at 30 min after injection) but more rapid clearance (1.82 ± 0.29 %ID/g vs. 2.01 ± 0.25 %ID/g at 1 h after injection) than ^{64}Cu -DOTA-RGD. The **integrin** receptor specificity of this radiotracer was demonstrated by blocking of tumor uptake by coinjection with nonradiolabeled c(RGDyK). The high tumor-to-organ ratios for the pegylated RGD peptide tracer (at 1 h after injection: tumor-to-blood ratio, 20; tumor-to-muscle ratio, 12; tumor-to-liver ratio, 2.7; and tumor-to-kidney ratio, 1.2) were confirmed by microPET and autoradiog. imaging in a s.c. U87MG tumor model. This tracer was also able to detect an orthotopic brain tumor in a model in which U87MG cells were implanted into the mouse forebrain. Although the magnitude of tumor uptake in the orthotopic **xenograft** was lower than that in the s.c. **xenograft**, the orthotopic tumor was still visualized with clear contrast from normal brain tissue. Conclusion: This study demonstrated the suitability of a PEG moiety for improving the in vivo kinetics of a ^{64}Cu -RGD peptide tracer without compromising the tumor-targeting ability and specificity of the peptide. Systematic investigations of the effects of the size and geometry of PEG on tumor targeting and in vivo kinetics will lead to the development of radiotracers suitable for clin. applications such as visualizing and quantifying αv - **integrin** expression by PET. In addition, the same ligand labeled with therapeutic radionuclides may be applicable for **integrin**-targeted internal radiotherapy.

CC 8-9 (Radiation Biochemistry)

Section cross-reference(s): 63

IT Drug delivery systems

(carriers; ^{64}Cu -DOTA-PEG-peptide conjugate for PET imaging of brain tumor $\alpha\text{v}\beta 3$ - **integrin** expression)

IT **Integrins**

RL: BSU (Biological study, unclassified); BIOL (Biological study)

($\alpha\text{v}\beta 3$; ^{64}Cu -DOTA-PEG-peptide conjugate for PET imaging of brain tumor $\alpha\text{v}\beta 3$ - **integrin** expression)

IT Brain, neoplasm

Human

Imaging agents

Positron-emission tomography

Radiopharmaceuticals

(^{64}Cu -DOTA-PEG-peptide conjugate for PET imaging of brain tumor

$\alpha v\beta 3$ - **integrin** expression)
IT Polyoxyalkylenes, biological studies
RL: DGN (Diagnostic use); PKT (Pharmacokinetics); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(⁶⁴Cu-DOTA-PEG-peptide conjugate for PET imaging of brain tumor
 $\alpha v\beta 3$ - **integrin** expression)
IT **848028-84-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(R⁶⁴Cu-DOTA-PEG-peptide conjugate for PET imaging of brain tumor
 $\alpha v\beta 3$ - **integrin** expression)
IT **852993-22-7**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(⁶⁴Cu-DOTA-PEG-peptide conjugate for PET imaging of brain tumor
 $\alpha v\beta 3$ - **integrin** expression)
IT **217099-14-4** 852993-20-5
RL: BSU (Biological study, unclassified); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent)
(⁶⁴Cu-DOTA-PEG-peptide conjugate for PET imaging of brain tumor
 $\alpha v\beta 3$ - **integrin** expression)
IT **852993-21-6P**
RL: BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(⁶⁴Cu-DOTA-PEG-peptide conjugate for PET imaging of brain tumor
 $\alpha v\beta 3$ - **integrin** expression)
IT 13981-25-4DP, Copper 64, PEGylated Arg-Gly-Asp peptide labeled with, biological studies 25322-68-3DP, PEG, ⁶⁴Cu-labeled Arg-Gly-Asp peptide conjugate **852995-19-8P**
RL: DGN (Diagnostic use); PKT (Pharmacokinetics); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(⁶⁴Cu-DOTA-PEG-peptide conjugate for PET imaging of brain tumor
 $\alpha v\beta 3$ - **integrin** expression)
IT 778648-12-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(⁶⁴Cu-DOTA-PEG-peptide conjugate for PET imaging of brain tumor
 $\alpha v\beta 3$ - **integrin** expression)
IT **848028-84-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(R⁶⁴Cu-DOTA-PEG-peptide conjugate for PET imaging of brain tumor
 $\alpha v\beta 3$ - **integrin** expression)
IT **852993-22-7**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(⁶⁴Cu-DOTA-PEG-peptide conjugate for PET imaging of brain tumor
 $\alpha v\beta 3$ - **integrin** expression)
IT **217099-14-4**
RL: BSU (Biological study, unclassified); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent)
(⁶⁴Cu-DOTA-PEG-peptide conjugate for PET imaging of brain tumor
 $\alpha v\beta 3$ - **integrin** expression)
IT **852993-21-6P**
RL: BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(⁶⁴Cu-DOTA-PEG-peptide conjugate for PET imaging of brain tumor
 $\alpha v\beta 3$ - **integrin** expression)
IT **852995-19-8P**

RL: DGN (Diagnostic use); PKT (Pharmacokinetics); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)

(⁶⁴Cu-DOTA-PEG-peptide conjugate for PET imaging of brain tumor $\alpha\text{v}\beta 3$ - integrin expression)

IT 848028-84-2P

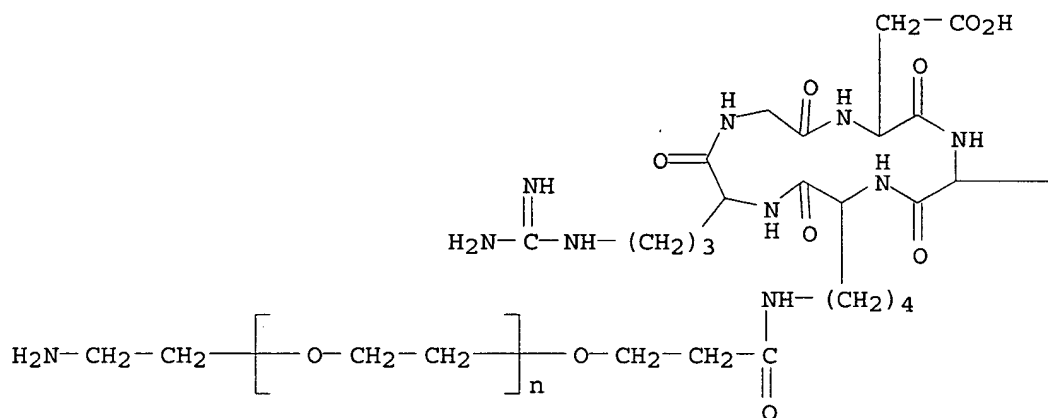
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(⁶⁴Cu-DOTA-PEG-peptide conjugate for PET imaging of brain tumor $\alpha\text{v}\beta 3$ - integrin expression)

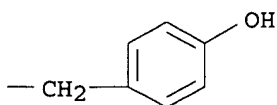
RN 848028-84-2 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), α -(2-aminoethyl)- ω -hydroxy-, 5-ether with cyclo[L-arginylglycyl-L- α -aspartyl-D-tyrosyl-N6-(3-hydroxy-1-oxopropyl)-L-lysyl] (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



IT 852993-22-7

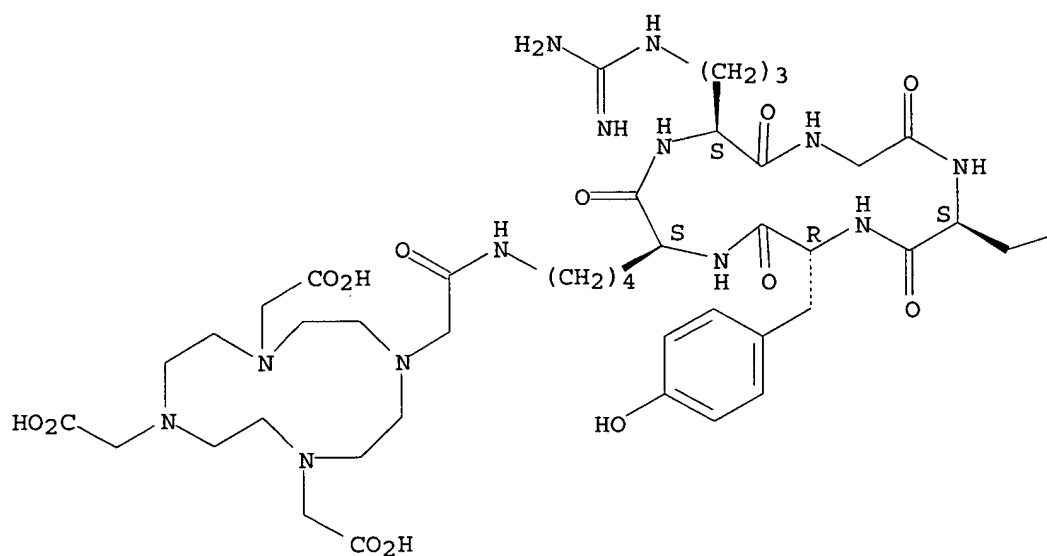
RL: BSU (Biological study, unclassified); BIOL (Biological study) (⁶⁴Cu-DOTA-PEG-peptide conjugate for PET imaging of brain tumor $\alpha\text{v}\beta 3$ - integrin expression)

RN 852993-22-7 HCAPLUS

CN Cyclo[L-arginylglycyl-L- α -aspartyl-D-tyrosyl-N6-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-L-lysyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

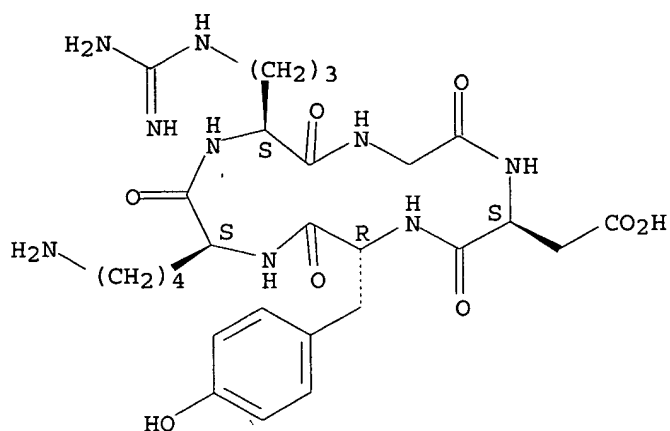


PAGE 1-B

—CO₂H

IT 217099-14-4
 RL: BSU (Biological study, unclassified); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent)
 (64Cu-DOTA-PEG-peptide conjugate for PET imaging of brain tumor
 αvβ3- **integrin** expression)
 RN 217099-14-4 HCAPLUS
 CN Cyclo(L-arginylglycyl-L-α-aspartyl-D-tyrosyl-L-lysyl) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 852993-21-6P

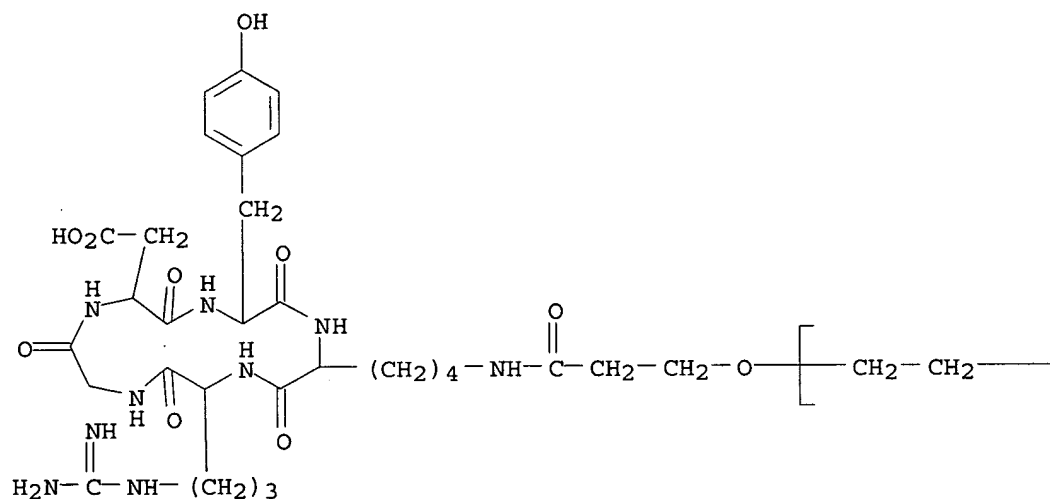
RL: BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)

(64Cu-DOTA-PEG-peptide conjugate for PET imaging of brain tumor $\alpha v \beta 3$ - integrin expression)

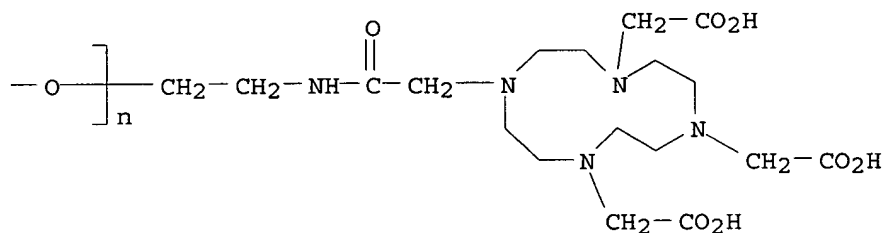
RN 852993-21-6 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), α -[2-[[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]amino]ethyl]- ω -hydroxy-, 5-ether with cyclo[L-arginylglycyl-L- α -aspartyl-D-tyrosyl-N6-(3-hydroxy-1-oxopropyl)-L-lysyl] (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



IT 852995-19-8P

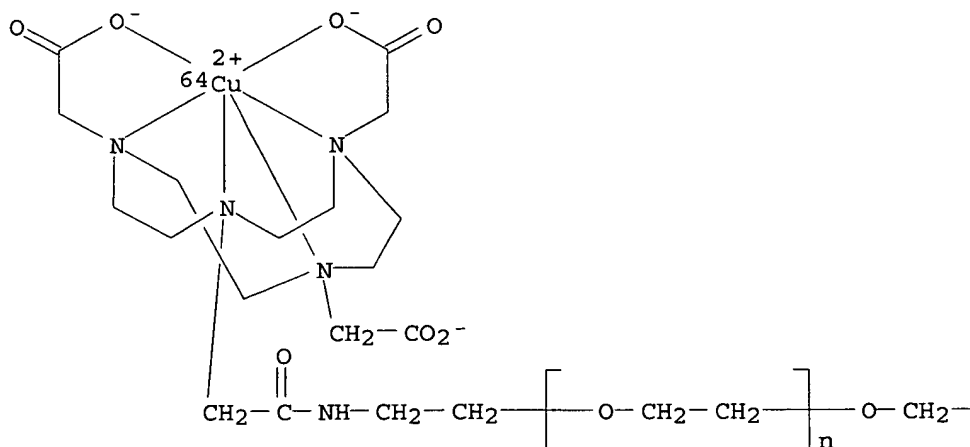
RL: DGN (Diagnostic use); PKT (Pharmacokinetics); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)

(⁶⁴Cu-DOTA-PEG-peptide conjugate for PET imaging of brain tumor
αvβ3- **integrin** expression)

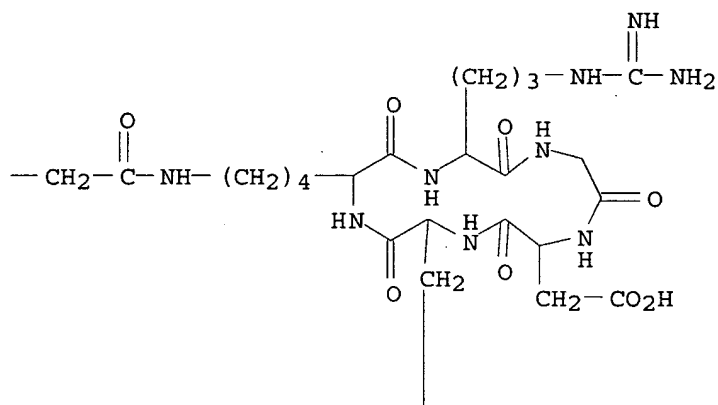
RN 852995-19-8 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), α-hydro-ω-hydroxy-, 5-ether with
cyclo[L-arginylglycyl-L-α-aspartyl-D-tyrosyl-N6-(3-hydroxy-1-oxopropyl)-L-lysyl], ether with hydrogen [10-[2-[(2-hydroxyethyl)amino]-2-oxoethyl]-1,4,7,10-tetraazacyclododecane-1,4,7-triacetato(3-)-κN1,κN4,κN7,κN10,κO1,κO4,κO7] cup
rate(1-)-⁶⁴Cu (9CI) (CA INDEX NAME)

PAGE 1-A



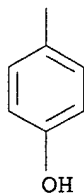
PAGE 1-B



PAGE 2-A

● H⁺

PAGE 2-B



REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 19 OF 43 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:913618 HCAPLUS

DOCUMENT NUMBER: 142:109507
 TITLE: In vivo Near-Infrared Fluorescence Imaging of **Integrin** $\alpha\text{v}\beta 3$ in Brain Tumor **Xenografts**
 AUTHOR(S): Chen, Xiaoyuan; Conti, Peter S.; Moats, Rex A.
 CORPORATE SOURCE: PET Imaging Science Center, University of Southern California Keck School of Medicine, Los Angeles, CA, USA
 SOURCE: Cancer Research (2004), 64(21), 8009-8014
 CODEN: CNREA8; ISSN: 0008-5472
 PUBLISHER: American Association for Cancer Research
 DOCUMENT TYPE: Journal
 LANGUAGE: English

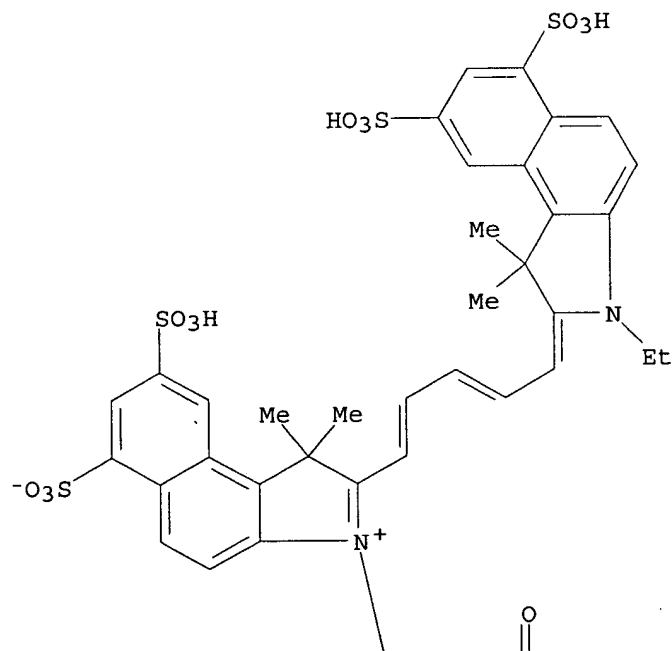
AB Noninvasive visualization of cell adhesion mol. $\alpha\text{v}\beta 3$ **integrin** expression in vivo has been well studied by using the radionuclide imaging modalities in various preclin. tumor models. A literature survey indicated no previous use of cyanine dyes as contrast agents for in vivo optical detection of tumor **integrin**. Herein, we report the **integrin** receptor specificity of novel peptide-dye conjugate arginine-glycine-aspartic acid (RGD)-Cy5.5 as a contrast agent in vitro, in vivo, and ex vivo. The RGD-Cy5.5 exhibited intermediate affinity for $\alpha\text{v}\beta 3$ **integrin** ($\text{IC}_{50} = 58.1 \pm 5.6$ nmol/L). The conjugate led to elevated cell-associated fluorescence on **integrin**-expressing tumor cells and endothelial cells and produced minimal cell fluorescence when coincubated with c(RGDyK). In vivo imaging with a prototype three-dimensional small-animal imaging system visualized s.c. U87MG glioblastoma **xenograft** with a broad range of concns. of fluorescent probe administered via the tail vein. The intermediate dose (0.5 nmol) produces better tumor contrast than high dose (3 nmol) and low dose (0.1 nmol) during 30 min to 24 h postinjection, because of partial self-inhibition of receptor-specific tumor uptake at high dose and the presence of significant amount of background fluorescence at low dose, resp. The tumor contrast was also dependent on the mouse viewing angles. Tumor uptake of RGD-Cy5.5 was blocked by unlabeled c(RGDyK). This study suggests that the combination of the specificity of RGD peptide/**integrin** interaction with near-IR fluorescence detection may be applied to noninvasive imaging of **integrin** expression and monitoring anti-**integrin** treatment efficacy providing near real-time measurements.

CC 8-9 (Radiation Biochemistry)
 ST nearIR fluorescence imaging agent RGD conjugate **integrin** brain tumor
 IT Fluorescence
 (IR; near-IR fluorescence imaging of **integrin** $\alpha\text{v}\beta 3$ in brain tumor)
 IT Imaging agents
 (contrast; near-IR fluorescence imaging of **integrin** $\alpha\text{v}\beta 3$ in brain tumor)
 IT Neuroglia, neoplasm
 (glioblastoma; near-IR fluorescence imaging of **integrin** $\alpha\text{v}\beta 3$ in brain tumor)
 IT Fluorescent indicators
 Human
 (near-IR fluorescence imaging of **integrin** $\alpha\text{v}\beta 3$ in brain tumor)
 IT Imaging
 (tumor; near-IR fluorescence imaging of **integrin** $\alpha\text{v}\beta 3$ in brain tumor)
 IT **Integrins**
 RL: BSU (Biological study, unclassified); BIOL (Biological study)

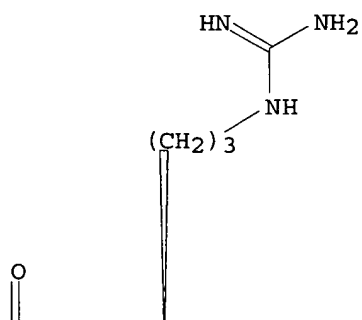
- ($\alpha\beta3$; near-IR fluorescence imaging of **integrin** $\alpha\beta3$ in brain tumor)
- IT **820967-21-3**, RGD-Cy 5.5
 RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (near-IR fluorescence imaging of **integrin** $\alpha\beta3$ in brain tumor)
- IT **820967-21-3**, RGD-Cy 5.5
 RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (near-IR fluorescence imaging of **integrin** $\alpha\beta3$ in brain tumor)
- IT **820967-21-3**, RGD-Cy 5.5
 RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (near-IR fluorescence imaging of **integrin** $\alpha\beta3$ in brain tumor)
- RN **820967-21-3** HCAPLUS
 CN Cyclo[L-arginylglycyl-L- α -aspartyl-D-tyrosyl-N6-[6-[2-[5-(3-ethyl-1,3-dihydro-1,1-dimethyl-6,8-disulfo-2H-benz[e]indol-2-ylidene)-1,3-pentadienyl]-1,1-dimethyl-6,8-disulfo-1H-benz[e]indolio]-1-oxohexyl]-L-lysyl], inner salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry unknown.

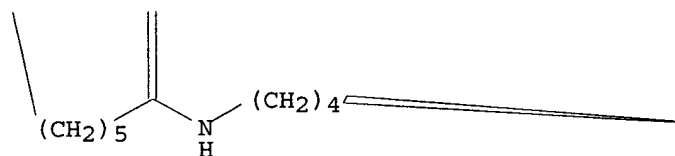
PAGE 1-A



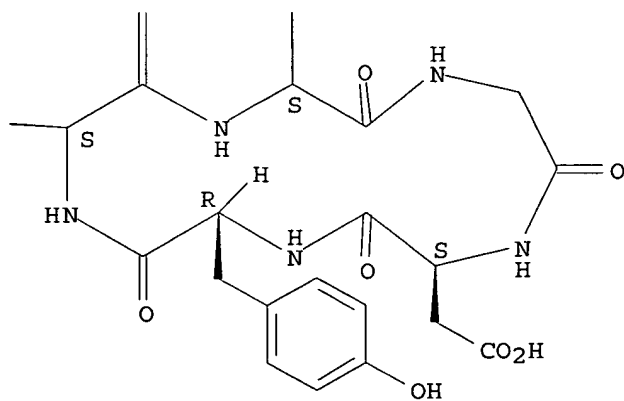
PAGE 1-B



PAGE 2-A



PAGE 2-B



REFERENCE COUNT:

36

THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 20 OF 43 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:913075 HCAPLUS

DOCUMENT NUMBER: 143:133666

TITLE: Chemoselective **Oxime** and Thiazolidine Bond
Formation: A Versatile and Efficient Route to the
Preparation of 3'-Peptide-Oligonucleotide Conjugates

AUTHOR(S): Villien, Mathilde; Defrancq, Eric; Dumy, Pascal

CORPORATE SOURCE: LEDSS, UMR CNRS 5616, Universite Joseph Fourier,
Grenoble, Fr.

SOURCE: Nucleosides, Nucleotides & Nucleic Acids (2004),
23(10), 1657-1666

CODEN: NNNAFY; ISSN: 1525-7770

PUBLISHER: Marcel Dekker, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 143:133666

AB An oligonucleotide carrying an aldehyde moiety at the 3'-end was
synthesized by the oxidation of a 1,2-diol precursor. This was coupled to
peptides bearing a cysteine residue for thiazolidine formation and an
aminoxy group for **oxime** formation. The conjugation reaction
proved very efficient and selective, thereby allowing the preparation of
3'-peptide-oligonucleotide conjugates in good yield. The conjugation was
achieved in aqueous solution without using any protection strategy. Moreover,
the present approach neither requires the use of peptide in excess nor
changes the hybridization properties of the conjugates.

CC 34-3 (Amino Acids, Peptides, and Proteins)

Section cross-reference(s): 33

ST peptide oligonucleotide **oxime** thiazolidine conjugate
chemoselective prepn

IT Oligonucleotides

RL: SPN (Synthetic preparation); PREP (Preparation)
(conjugates, 3'-peptide; preparation of 3'-peptide-oligonucleotide
conjugates via chemoselective **oxime** and thiazolidine bond
formation)

IT 151427-58-6D, aminoalkylated controlled pore glass-bound 388633-56-5
388633-59-8 858124-61-5 858124-62-6

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of 3'-peptide-oligonucleotide conjugates via chemoselective
oxime and thiazolidine bond formation)

IT 858682-81-2P 858981-44-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)

(preparation of 3'-peptide-oligonucleotide conjugates via chemoselective
oxime and thiazolidine bond formation)

IT 858682-82-3P 858981-45-0P 858981-46-1P 858981-47-2P

RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation of 3'-peptide-oligonucleotide conjugates via chemoselective
oxime and thiazolidine bond formation)

IT 858124-61-5 858124-62-6

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of 3'-peptide-oligonucleotide conjugates via chemoselective
oxime and thiazolidine bond formation)

IT 858124-61-5 858124-62-6

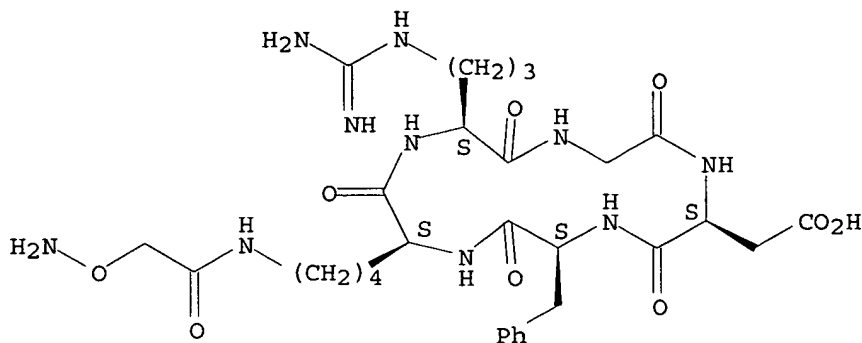
RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of 3'-peptide-oligonucleotide conjugates via chemoselective
oxime and thiazolidine bond formation)

RN 858124-61-5 HCAPLUS

CN Cyclo[L-arginylglycyl-L- α -aspartyl-L-phenylalanyl-N6-
[(aminoxy)acetyl]-L-lysyl] (9CI) (CA INDEX NAME)

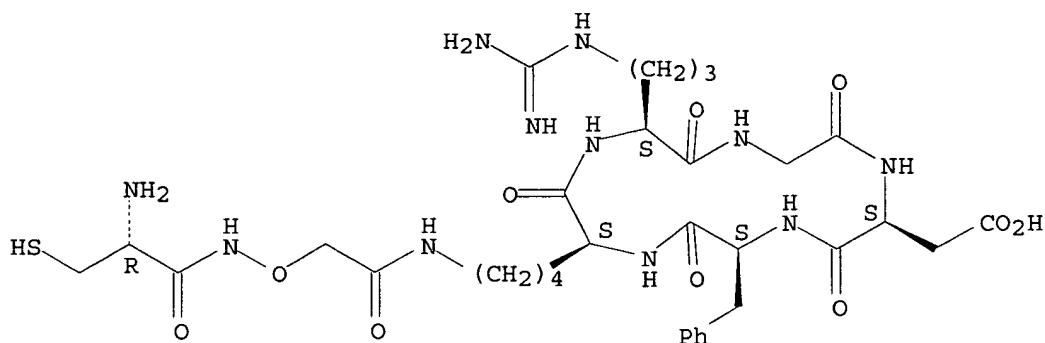
Absolute stereochemistry.



RN 858124-62-6 HCAPLUS

CN Cyclo[L-arginylglycyl-L-α-aspartyl-L-phenylalanyl-N6-[L-cysteinyl (aminooxy)acetyl]-L-lysyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 21 OF 43 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:777609 HCAPLUS

DOCUMENT NUMBER: 142:425974

TITLE: Improved Tumor Targeting of Radiolabeled RGD Peptides Using Rapid Dose Fractionation

AUTHOR(S): Janssen, Marcel; Frielink, Cathelijne; Dijkgraaf, Ingrid; Oyen, Wim; Edwards, D. Scott; Liu, Shuang; Rajopadhye, Milind; Massuger, Leon; Corstens, Frans; Boerman, Otto

CORPORATE SOURCE: Department of Nuclear Medicine, university Medical Center Nijmegen, Nijmegen, 6500 HB, Neth.

SOURCE: Cancer Biotherapy & Radiopharmaceuticals (2004), 19(4), 399-404

CODEN: CBRAFJ; ISSN: 1084-9785

PUBLISHER: Mary Ann Liebert, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Arginine-glycine-aspartic acid (RGD) peptides preferentially bind to αvβ3 integrin, an integrin expressed on newly formed endothelial cells and on various tumor cells. When labeled

with -emitting radionuclides; these peptides can be used for peptide-receptor radionuclide therapy of malignant tumors. These studies aimed to investigate whether tumor targeting and tumor therapy could be optimized by dose fractionation. The RGD-peptide DOTA-E-[c(RGDfK)]₂ was labeled with ¹¹¹In for biodistribution expts. and with ⁹⁰Y for therapy expts. In mice with NIH:OVCA-3 ovarian carcinoma **xenografts**, optimal tumor uptake was obtained at peptide doses up to 1.0 g (4.8 %ID/g). A peptide dose of 5 g, required to administer the maximum tolerable dose (MTD) ⁹⁰Y-DOTA-E-[c(RGDfK)]₂, was administered as 5 portions of 1.0 g. Tumor uptake of the fifth portion was significantly higher than that of the single 5.0 g portion (3.3 %ID/g vs. 2.1 %ID/g). The therapeutic efficacy of 37 MBq ⁹⁰Y-DOTA-E-[c(RGDfK)]₂ (1 x 5.0 g) was compared with that of 37 MBq administered in five equal portions (5 x 1.0 g). No difference in tumor growth between the fractionated and the nonfractionated therapy was observed. In conclusion, dose fractionation resulted in higher radiation doses. However, therapeutic efficacy of the radiolabeled peptide was not significantly improved by dose fractionation.

CC 8-9 (Radiation Biochemistry)

Section cross-reference(s): 63

ST tumor targeted radiolabeled RGD peptide dose fractionation; RGD peptide **integrin** targeted radiotherapy tumor

IT Ovary, neoplasm

(carcinoma; improved ovarian tumor **integrin** targeting of radiolabeled RGD peptides using rapid dose fractionation)

IT Antitumor agents

Human

(improved ovarian tumor **integrin** targeting of radiolabeled RGD peptides using rapid dose fractionation)

IT Carcinoma

(ovarian; improved ovarian tumor **integrin** targeting of radiolabeled RGD peptides using rapid dose fractionation)

IT Radiotherapy

(targeted; improved ovarian tumor **integrin** targeting of radiolabeled RGD peptides using rapid dose fractionation)

IT **Integrins**

RL: BSU (Biological study, unclassified); BIOL (Biological study)

($\alpha v \beta 3$; improved ovarian tumor **integrin** targeting of radiolabeled RGD peptides using rapid dose fractionation)

IT 851024-71-0

RL: DGN (Diagnostic use); PKT (Pharmacokinetics); BIOL (Biological study); USES (Uses)

(improved ovarian tumor **integrin** targeting of radiolabeled RGD peptides using rapid dose fractionation)

IT 250614-38-1

RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU

(Therapeutic use); BIOL (Biological study); USES (Uses)

(improved ovarian tumor **integrin** targeting of radiolabeled RGD peptides using rapid dose fractionation)

IT 851024-71-0

RL: DGN (Diagnostic use); PKT (Pharmacokinetics); BIOL (Biological study); USES (Uses)

(improved ovarian tumor **integrin** targeting of radiolabeled RGD peptides using rapid dose fractionation)

IT 250614-38-1

RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU

(Therapeutic use); BIOL (Biological study); USES (Uses)

(improved ovarian tumor **integrin** targeting of radiolabeled RGD peptides using rapid dose fractionation)

IT 851024-71-0

RL: DGN (Diagnostic use); PKT (Pharmacokinetics); BIOL (Biological study);

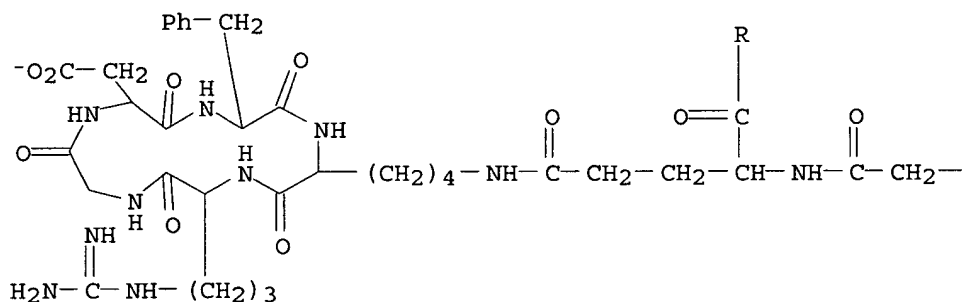
USES (Uses)

(improved ovarian tumor **integrin** targeting of radiolabeled RGD peptides using rapid dose fractionation)

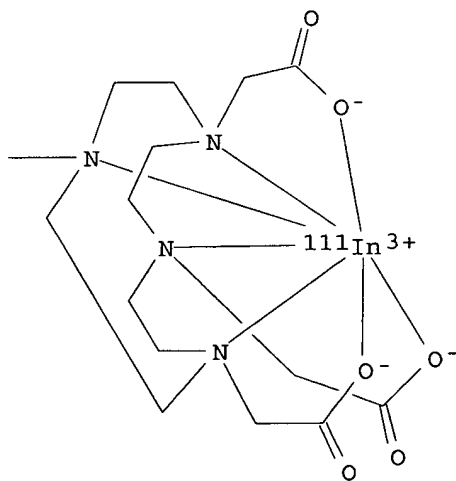
RN 851024-71-0 HCAPLUS

CN Indate(2-)-¹¹¹In, [[5,5'-(N-[[4,7,10-tris[(carboxy-κO)methyl]-1,4,7,10-tetraazacyclododec-1-yl-κN1,κN4,κN7,κN10]acetyl]-L-glutamoyl]bis[cyclo[L-arginylglycyl-L-α-aspartyl-D-phenylalanyl-L-lysylato]](5-)]-, dihydrogen (9CI) (CA INDEX NAME)

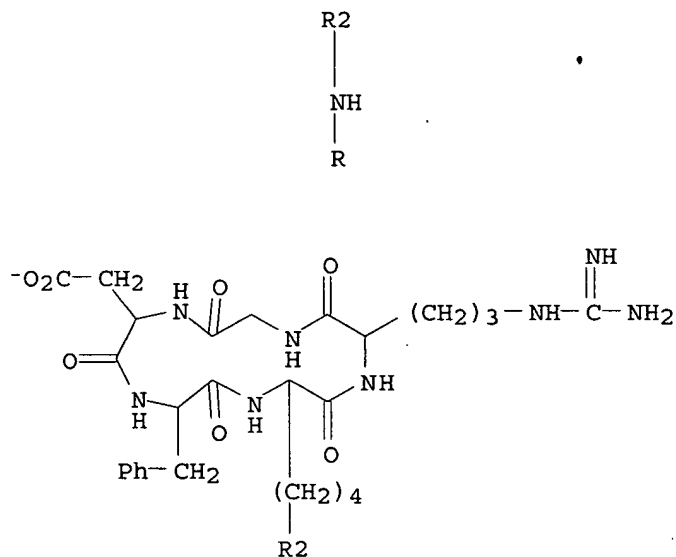
PAGE 1-A



PAGE 1-B



PAGE 2-A



PAGE 2-B

● 2 H⁺

IT 250614-38-1

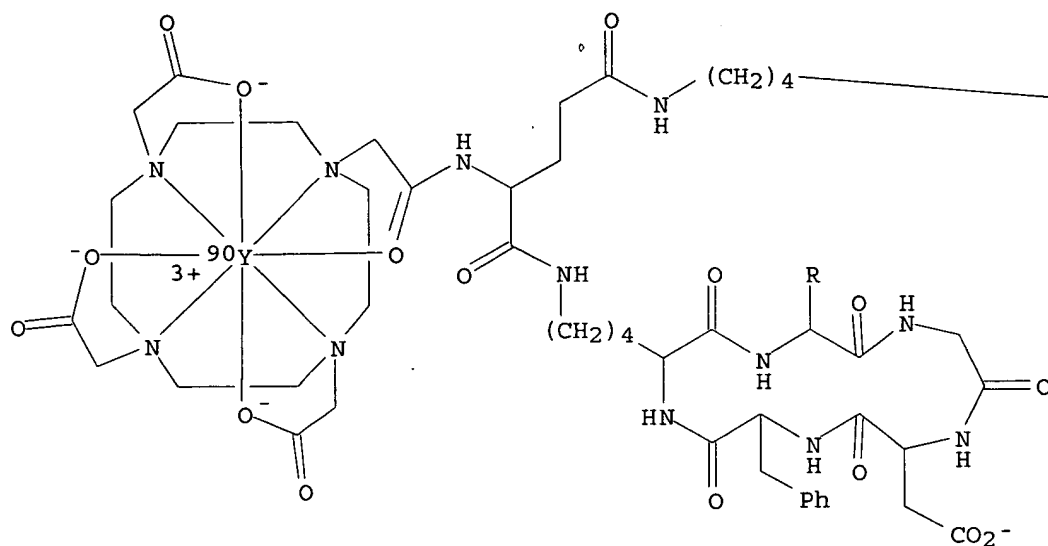
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(improved ovarian tumor **integrin** targeting of radiolabeled RGD peptides using rapid dose fractionation)

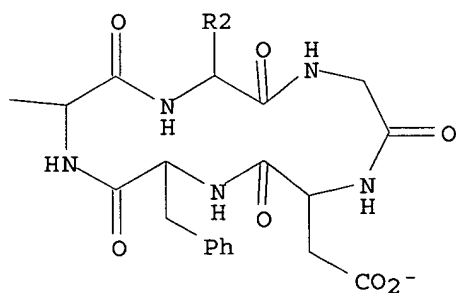
RN 250614-38-1 HCAPLUS

CN Yttrate(2-)-90Y, [[5,5'-[N-[4,7,10-tris[(carboxy-κO)methyl]-1,4,7,10-tetraazacyclododec-1-yl-κN1,κN4,κN7,κN10]acetyl-κO]-L-glutamoyl]bis[cyclo(L-arginylglycyl-L-α-aspartyl-D-phenylalanyl-L-lysylato)]](5-)]-, dihydrogen (9CI) (CA INDEX NAME)

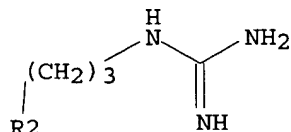
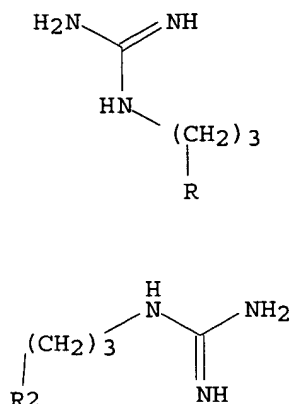
PAGE 1-A



PAGE 1-B



PAGE 2-A

● 2 H⁺

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 22 OF 43 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:594195 HCAPLUS

DOCUMENT NUMBER: 142:235597

TITLE: Micro-PET imaging of $\alpha v \beta 3$ - **integrin** expression with 18F-labeled dimeric RGD peptide

AUTHOR(S): Chen, Xiaoyuan; Tohme, Michel; Park, Ryan; Hou, Yingping; Bading, James R.; Conti, Peter S.

CORPORATE SOURCE: University of Southern California, USA

SOURCE: Molecular Imaging (2004), 3(2), 96-104

CODEN: MIOMBP; ISSN: 1535-3508

PUBLISHER: MIT Press

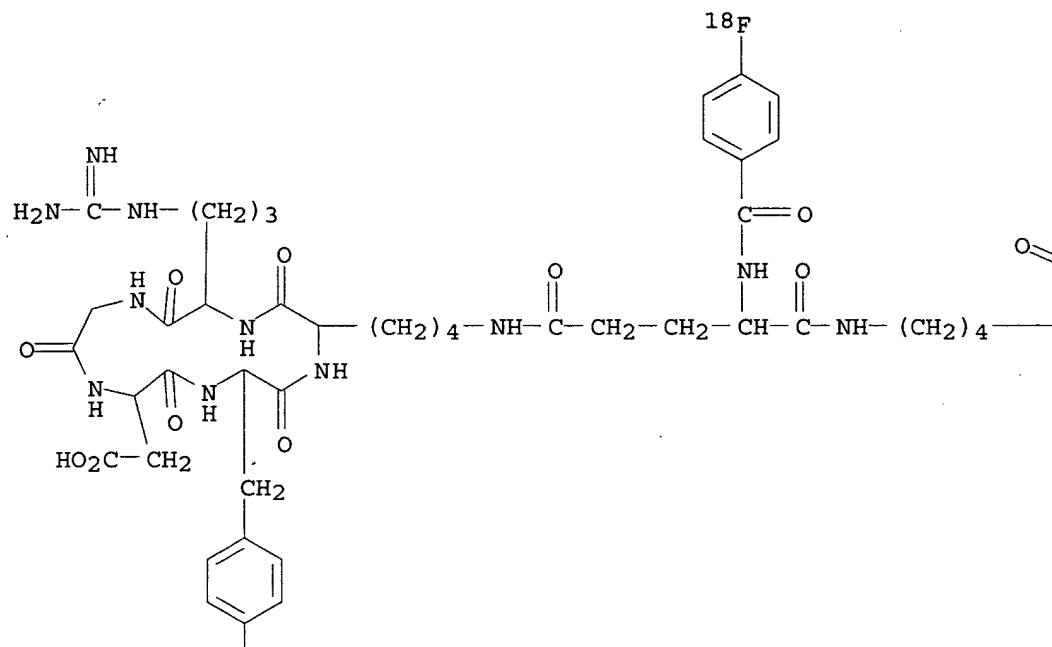
DOCUMENT TYPE: Journal

LANGUAGE: English

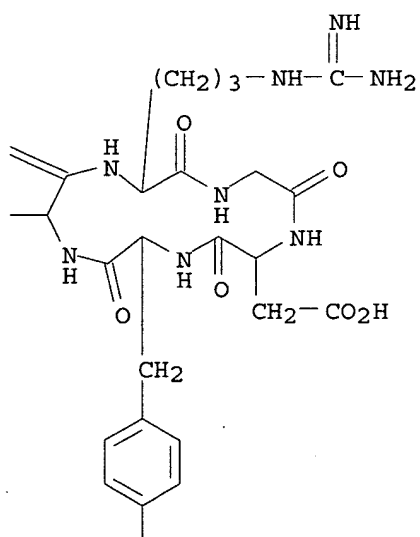
AB The αv **integrins**, which act as cell adhesion mols., are closely involved with tumor invasion and angiogenesis. In particular, $\alpha v \beta 3$ which is specifically expressed on proliferating endothelial cells and tumor cells, is a logical target for development of a radiotracer method to assess angiogenesis and anti-angiogenic therapy. In this study, a dimeric cyclic RGD peptide E[c(RGDyK)]₂ was labeled with 18F (t_{1/2} = 109.7 min) by using a prosthetic 4-[18F]fluorobenzoyl moiety to the amino group of the glutamate. The resulting [18F]FB-E[c(RGDyK)]₂, with high specific activity (200-250 GBq/ μ mol at the end of synthesis), was administered to s.c. U87MG glioblastoma **xenograft** models for micro-PET and autoradiog. imaging as well as direct tissue sampling to assess tumor targeting efficacy and in vivo kinetics of this PET tracer. The dimeric RGD peptide demonstrated significantly higher tumor uptake and prolonged tumor retention in comparison with a monomeric RGD peptide analog [18F]FB-c(RGDyK). The dimeric RGD peptide had predominant renal excretion, whereas the monomeric analog was excreted primarily through the biliary route. Micro-PET imaging 1 h after injection of the dimeric RGD peptide exhibited tumor to contralateral background ratio of 9.5 \pm 0.8. The synergistic effect of polyvalency and improved pharmacokinetics may be responsible for the superior imaging characteristics of [18F]FB-E[c(RGDyK)]₂.

CC 8-9 (Radiation Biochemistry)
 ST PET imaging alphavbeta3 **integrin** fluorine dimeric RGD peptide
 IT Neuroglia, neoplasm
 (glioblastoma; micro-PET imaging of $\alpha\text{v}\beta 3$ - **integrin**
 expression with 18F-labeled dimeric RGD peptide)
 IT Human
 Imaging agents
 Neoplasm
 Positron-emission tomography
 (micro-PET imaging of $\alpha\text{v}\beta 3$ - **integrin** expression
 with 18F-labeled dimeric RGD peptide)
 IT RGD peptides
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (micro-PET imaging of $\alpha\text{v}\beta 3$ - **integrin** expression
 with 18F-labeled dimeric RGD peptide)
 IT Drug interactions
 (synergistic; micro-PET imaging of $\alpha\text{v}\beta 3$ - **integrin**
 expression with 18F-labeled dimeric RGD peptide)
 IT Biological transport
 (uptake; micro-PET imaging of $\alpha\text{v}\beta 3$ - **integrin**
 expression with 18F-labeled dimeric RGD peptide)
 IT **Integrins**
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 ($\alpha\text{v}\beta 3$; micro-PET imaging of $\alpha\text{v}\beta 3$ - **integrin**
 expression with 18F-labeled dimeric RGD peptide)
 IT **844874-12-0P**
 RL: DGN (Diagnostic use); PKT (Pharmacokinetics); SPN (Synthetic
 preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (micro-PET imaging of $\alpha\text{v}\beta 3$ - **integrin** expression
 with 18F-labeled dimeric RGD peptide)
 IT 13981-56-1, F 18, reactions
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (micro-PET imaging of $\alpha\text{v}\beta 3$ - **integrin** expression
 with 18F-labeled dimeric RGD peptide)
 IT **844874-12-0P**
 RL: DGN (Diagnostic use); PKT (Pharmacokinetics); SPN (Synthetic
 preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (micro-PET imaging of $\alpha\text{v}\beta 3$ - **integrin** expression
 with 18F-labeled dimeric RGD peptide)
 IT **844874-12-0P**
 RL: DGN (Diagnostic use); PKT (Pharmacokinetics); SPN (Synthetic
 preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (micro-PET imaging of $\alpha\text{v}\beta 3$ - **integrin** expression
 with 18F-labeled dimeric RGD peptide)
 RN 844874-12-0 HCAPLUS
 CN Cyclo(L-arginylglycyl-L- α -aspartyl-D-tyrosyl-L-lysyl),
 5,5'-[N-[4-(fluoro-18F)benzoyl]-L-glutamoyl]bis- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



PAGE 2-A

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OH

PAGE 2-B

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OH

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 23 OF 43 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:507442 HCAPLUS

DOCUMENT NUMBER: 142:43629

TITLE: **Grafting** RGD containing peptides onto hydroxyapatite to promote osteoblastic cells adhesion
AUTHOR(S): Durrieu, M. C.; Pallu, S.; Guillemot, F.; Bareille, R.; Amedee, J.; Baquey, Ch.; Labrugere, C.; Dard, M.
CORPORATE SOURCE: "Biomateriaux et Reparation Tissulaire", INSERM U577, Bordeaux, 33076, Fr.

SOURCE: Journal of Materials Science: Materials in Medicine (2004), 15(7), 779-786

CODEN: JSMREL; ISSN: 0957-4530

PUBLISHER: Kluwer Academic Publishers

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Ceramics possess osteoconductive properties but exhibit no intrinsic osteoinductive capacity. Consequently, they are unable to induce new bone formation in extra osseous sites. In order to develop bone substitutes with osteogenic properties, one promising approach consists of creating hybrid materials by associating in vitro biomaterials with osteoprogenitor cells. With this aim, we have developed a novel strategy of biomimetic modification to enhance osseointegration of hydroxyapatite (HA) implants. RGD-containing peptides displaying different conformations (linear GRGDSPC and cyclo-DfKRG) were **grafted** onto HA surface by means of a three-step reaction procedure: silanization with APTES, crosslinking with N-succinimidyl-3-maleimidopropionate and finally immobilization of peptides thanks to thiol bonding. Whole process was performed in anhydrous conditions to ensure the reproducibility of the chemical functionalization. The three-step reaction procedure was characterized by high resolution XPS. Efficiency of this biomimetic modification was finally demonstrated by measuring the adhesion of osteoprogenitor cells isolated from HBMSC onto HA surface.

CC 63-7 (Pharmaceuticals)

IT Bone

(artificial; **grafting** RGD containing peptides onto hydroxyapatite to promote osteoblastic cells adhesion)

IT Adhesion, biological

Bone formation

Immobilization, molecular or cellular

Osteoblast

(**grafting** RGD containing peptides onto hydroxyapatite to promote osteoblastic cells adhesion)

IT RGD peptides

RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (grafting RGD containing peptides onto hydroxyapatite to promote osteoblastic cells adhesion)

IT Prosthetic materials and Prosthetics
 (implants; grafting RGD containing peptides onto hydroxyapatite to promote osteoblastic cells adhesion)

IT 181786-27-6
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (grafting RGD containing peptides onto hydroxyapatite to promote osteoblastic cells adhesion)

IT 1306-06-5, Hydroxyapatite
 RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (grafting RGD containing peptides onto hydroxyapatite to promote osteoblastic cells adhesion)

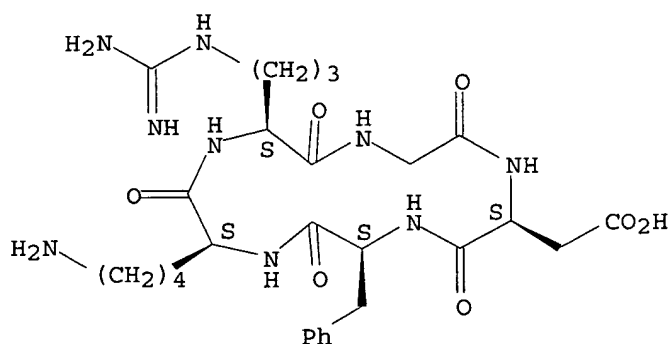
IT 919-30-2, 3-Aminopropyltriethoxysilane 55750-62-4, N-Succinimidyl-3-maleimidopropionate
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (grafting RGD containing peptides onto hydroxyapatite to promote osteoblastic cells adhesion)

IT 181786-27-6
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (grafting RGD containing peptides onto hydroxyapatite to promote osteoblastic cells adhesion)

IT 181786-27-6
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (grafting RGD containing peptides onto hydroxyapatite to promote osteoblastic cells adhesion)

RN 181786-27-6 HCAPLUS
 CN Cyclo(L-arginylglycyl-L- α -aspartyl-L-phenylalanyl-L-lysyl) (9CI)
 (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 24 OF 43 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:412755 HCAPLUS

DOCUMENT NUMBER: 141:5810

TITLE: Differentially expressed genes and encoded proteins in differentiated macrophages that are useful for

diagnosis and treatment of immune-related diseases
 INVENTOR(S): Clark, Hilary; Schoenfeld, Jill; Van Lookeren, Menno;
 PATENT ASSIGNEE(S): Williams, P. Mickey; Wood, William I.; Wu, Thomas D.
 SOURCE: Genentech, Inc., USA
 PCT Int. Appl., 2940 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004041170	A2	20040521	WO 2003-US34312	20031030
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2503390	AA	20040521	CA 2003-2503390	20031030
AU 2003284357	A1	20040607	AU 2003-284357	20031030
EP 1578367	A2	20050928	EP 2003-776595	20031030
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2006515747	T2	20060608	JP 2004-550183	20031030
PRIORITY APPLN. INFO.:			US 2002-423394P	P 20021101
			WO 2003-US34312	W 20031030
AB	The present invention relates to compns. containing novel proteins and methods of using those compns. for the diagnosis and treatment of immune-related diseases. Specific cDNA sequences are provided which are differentially expressed (up-regulated) in differentiated macrophages at day 7 as compared to normal undifferentiated monocytes at day 0 and day 1. The encoded proteins are useful not only as diagnostic markers for the presence of one or more immune disorders, but also serve as therapeutic targets for the treatment of those immune disorders and inflammatory immune responses..			
IC	ICM A61K			
CC	15-7 (Immunochemistry)			
IT	Section cross-reference(s): 1, 3, 6, 9			
IT	Transplant and Transplantation (graft-vs.-host reaction; differentially expressed genes and encoded proteins in differentiated macrophages that are useful for diagnosis and treatment of immune-related diseases)			
IT	212756-87-1	678990-33-5	688739-47-1	688739-48-2
	694503-21-4	694535-05-2	694535-07-4	694535-09-6
	694535-13-2	694535-15-4	694535-17-6	694535-19-8
	694535-23-4	694535-25-6	694535-27-8	694535-29-0
	694535-33-6	694535-35-8	694535-37-0	694535-39-2
	694535-43-8	694535-45-0	694535-47-2	694535-49-4
	694535-54-1	694535-56-3	694535-58-5	694535-60-9
	694535-64-3	694535-66-5	694535-68-7	694535-70-1
	694535-74-5	694535-76-7	694535-78-9	694535-80-3
	694535-85-8	694535-87-0	694535-89-2	694535-91-6
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694536-45-3	694536-47-5	694536-49-7	694536-51-1	694536-54-4
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694536-87-3	694536-89-5	694536-91-9	694536-93-1	694536-95-3
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694537-10-5	694537-12-7	694537-14-9	694537-16-1	694537-18-3
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694539-23-6	694539-25-8	694539-28-1	694539-30-5	694539-32-7
694539-34-9	694539-36-1	694539-38-3	694539-40-7	694539-42-9
694539-44-1	694539-46-3	694539-48-5	694539-50-9	694539-52-1
694539-54-3	694539-56-5	694539-58-7	694539-60-1	694539-63-4
694539-65-6	694539-67-8	694539-69-0	694539-71-4	

RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (amino acid sequence; differentially expressed genes and encoded proteins in differentiated macrophages that are useful for diagnosis and treatment of immune-related diseases)

IT **694539-32-7**

RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (amino acid sequence; differentially expressed genes and encoded proteins in differentiated macrophages that are useful for diagnosis and treatment of immune-related diseases)

IT **694539-32-7**

RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (amino acid sequence; differentially expressed genes and encoded proteins in differentiated macrophages that are useful for diagnosis and treatment of immune-related diseases)

RN 694539-32-7 HCAPLUS

CN Immune-related disease-associated protein PRO59326 (human) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L47 ANSWER 25 OF 43 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:362570 HCAPLUS

DOCUMENT NUMBER: 141:123852
TITLE: The **oxime** bond formation as an efficient chemical tool for the preparation of 3',5'-bi-functionalized oligodeoxyribonucleotides
AUTHOR(S): Edupuganti, Om Prakash; Renaudet, Olivier; Defrancq, Eric; Dumy, Pascal
CORPORATE SOURCE: ICMG FR2607, UMR CNRS 5616, LEDSS, Universite Joseph Fourier, Grenoble, 38041, Fr.
SOURCE: Bioorganic & Medicinal Chemistry Letters (2004), 14(11), 2839-2842
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 141:123852

AB The simultaneous conjugation of peptides or carbohydrates at the 3'- and 5'-end of oligodeoxyribonucleotides was achieved very efficiently through chemoselective **oxime** bond formation. The method employs bi-functionalized oligonucleotides in single step without the need of protection strategy, under mild acidic conditions. The conjugates were obtained in high yields by reacting an oxy-amine containing reporter groups (peptide, mono- and disaccharide) with an oligonucleotide carrying an aldehyde at each extremity.

CC 33-10 (Carbohydrates)
Section cross-reference(s): 34

ST **oxime** aldehyde oligodeoxyribonucleotide prepn peptide
IT Oligodeoxyribonucleotides
Peptides, preparation
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(**oxime** bond formation as an efficient chemical tool for the preparation of peptide-containing 3',5'-bi-functionalized oligodeoxyribonucleotides)

IT 162848-39-7 215037-65-3 **343312-27-6** 388633-56-5
390756-39-5 627904-36-3D, CPG polymer support
RL: RCT (Reactant); RACT (Reactant or reagent)
(**oxime** bond formation as an efficient chemical tool for the preparation of peptide-containing 3',5'-bi-functionalized oligodeoxyribonucleotides)

IT 722555-50-2P 723343-93-9P 723343-94-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(**oxime** bond formation as an efficient chemical tool for the preparation of peptide-containing 3',5'-bi-functionalized oligodeoxyribonucleotides)

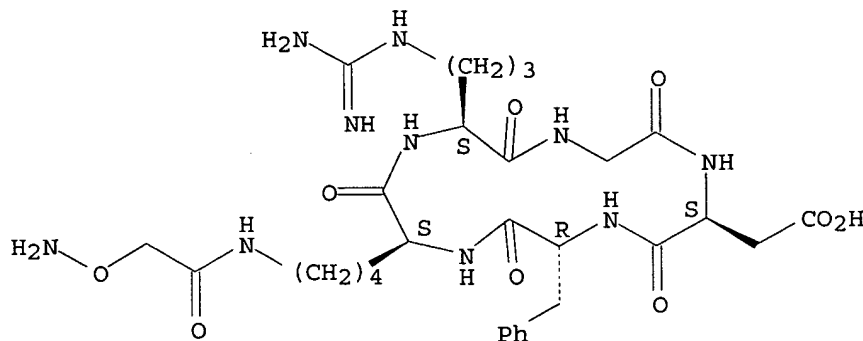
IT 722555-51-3P 723343-95-1P 723343-96-2P 723343-97-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(**oxime** bond formation as an efficient chemical tool for the preparation of peptide-containing 3',5'-bi-functionalized oligodeoxyribonucleotides)

IT **343312-27-6**
RL: RCT (Reactant); RACT (Reactant or reagent)
(**oxime** bond formation as an efficient chemical tool for the preparation of peptide-containing 3',5'-bi-functionalized oligodeoxyribonucleotides)

IT **343312-27-6**
RL: RCT (Reactant); RACT (Reactant or reagent)
(**oxime** bond formation as an efficient chemical tool for the preparation of peptide-containing 3',5'-bi-functionalized oligodeoxyribonucleotides)

RN 343312-27-6 HCAPLUS
 CN Cyclo[L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-N6-
 [(aminooxy)acetyl]-L-lysyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 26 OF 43 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:357447 HCAPLUS

DOCUMENT NUMBER: 142:120345

TITLE: Cyclo-(DfKRG) peptide **grafting** onto
 Ti-6Al-4V: physical characterization and interest
 towards human osteoprogenitor cells adhesion

AUTHOR(S): Porte-Durrieu, M. C.; Guillemot, F.; Pallu, S.;
 Labrugere, C.; Brouillaud, B.; Bareille, R.; Amedee,
 J.; Barthe, N.; Dard, M.; Baquey, Ch.

CORPORATE SOURCE: "Biomateriaux et RepARATION Tissulaire", INSERM U577,
 Bordeaux, 33076, Fr.

SOURCE: Biomaterials (2004), 25(19), 4837-4846
 CODEN: BIMADU; ISSN: 0142-9612

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB In the present paper, specific interest has been devoted to the design of
 new hybrid materials associating Ti-6Al-4V alloy and osteoprogenitor cells
 through the **grafting** of two RGD containing peptides displaying a
 different conformation (linear RGD and cyclo-DfKRG) onto titanium surface.
 Biomimetic modification was performed by means of a three-step reaction
 procedure: silanization with APTES, crosslinking with SMP and finally
 immobilization of peptides thanks to thiol bonding. The whole process was
 performed in anhydrous conditions to ensure homogeneous biomols. layout as
 well as to guarantee a sufficient amount of biomols. **grafted** onto
 surfaces. The efficiency of this new route for biomimetic modification of
 titanium surface was demonstrated by measuring the adhesion between 1 and
 24 h of osteoprogenitor cells isolated from HBMSC. Benefits of the
 as-proposed method were related to the high concentration of peptides
grafted onto the surface (around 20 pmol/mm²) as well as to the
 capacity of cyclo-DfKRG peptide to interact with **integrin**
 receptors. Moreover, High Resolution β -imager (using [35S]-Cys) has
 exhibited the stability of peptides **grafted** onto the surface
 when treated in harsh conditions.

CC 63-7 (Pharmaceuticals)

ST RGDC cyclic peptide **graft** Ti6Al4V prosthetic implant
 osteoprogenitor adhesion

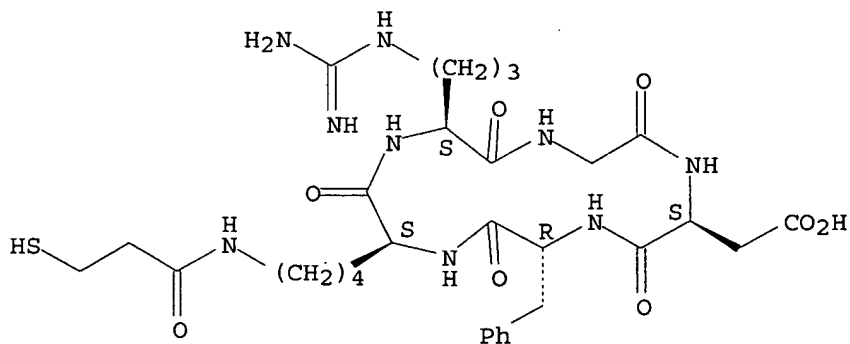
- IT Prosthetic materials and Prosthetics
(implants; linear RGDC and cyclic peptide **grafting** onto Ti-6Al-4V for human osteoprogenitor cell adhesion)
- IT Adhesion, biological
Human
Surface treatment
X-ray photoelectron spectroscopy
(linear RGDC and cyclic peptide **grafting** onto Ti-6Al-4V for human osteoprogenitor cell adhesion)
- IT Bone marrow
(osteoprogenitor cell; linear RGDC and cyclic peptide **grafting** onto Ti-6Al-4V for human osteoprogenitor cell adhesion)
- IT 12743-70-3DP, Ti-6Al-4V, surface reaction products with silane and succinimidyl propionate and cyclic peptides **190072-28-7DP**, surface reaction products with functionalized titanium alloy
RL: BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(linear RGDC and cyclic peptide **grafting** onto Ti-6Al-4V for human osteoprogenitor cell adhesion)
- IT 109292-46-8DP, reaction products with surface functionalized titanium alloy
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(linear RGDC and cyclic peptide **grafting** onto Ti-6Al-4V for human osteoprogenitor cell adhesion)
- IT 12743-70-3, Ti-6Al-4V
RL: CPS (Chemical process); PEP (Physical, engineering or chemical process); RCT (Reactant); PROC (Process); RACT (Reactant or reagent)
(linear RGDC and cyclic peptide **grafting** onto Ti-6Al-4V for human osteoprogenitor cell adhesion)
- IT 919-30-2, Aminopropyltriethoxysilane 55750-62-4 **190072-28-7**
RL: RCT (Reactant); RACT (Reactant or reagent)
(linear RGDC and cyclic peptide **grafting** onto Ti-6Al-4V for human osteoprogenitor cell adhesion)
- IT 919-30-2DP, Aminopropyltriethoxysilane, surface reaction products with titanium alloy and succinimidyl propionate 55750-62-4DP, reaction products with triethoxysilane and cyclic peptides
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(linear RGDC and cyclic peptide **grafting** onto Ti-6Al-4V for human osteoprogenitor cell adhesion)
- IT **190072-28-7DP**, surface reaction products with functionalized titanium alloy
RL: BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(linear RGDC and cyclic peptide **grafting** onto Ti-6Al-4V for human osteoprogenitor cell adhesion)
- IT **190072-28-7**
RL: RCT (Reactant); RACT (Reactant or reagent)
(linear RGDC and cyclic peptide **grafting** onto Ti-6Al-4V for human osteoprogenitor cell adhesion)
- IT **190072-28-7DP**, surface reaction products with functionalized titanium alloy
RL: BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(linear RGDC and cyclic peptide **grafting** onto Ti-6Al-4V for

human osteoprogenitor cell adhesion)

RN 190072-28-7 HCAPLUS

CN Cyclo[L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-N6-(3-mercapto-1-oxopropyl)-L-lysyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 190072-28-7

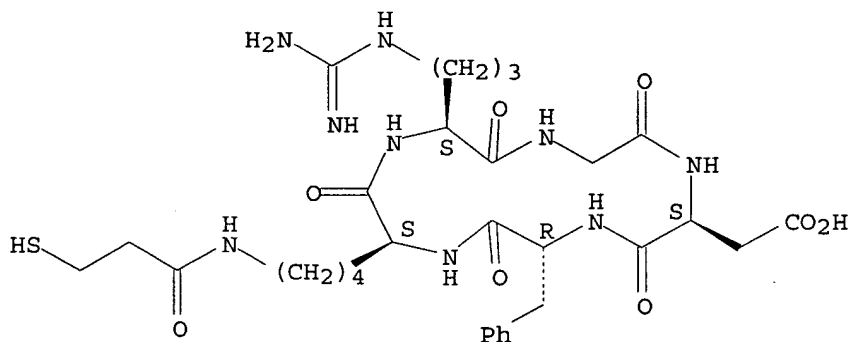
RL: RCT (Reactant); RACT (Reactant or reagent)

(linear RGDC and cyclic peptide **grafting** onto Ti-6Al-4V for human osteoprogenitor cell adhesion)

RN 190072-28-7 HCAPLUS

CN Cyclo[L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-N6-(3-mercapto-1-oxopropyl)-L-lysyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 27 OF 43 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:60559 HCAPLUS

DOCUMENT NUMBER: 140:122831

TITLE: Cytotoxic tissue factor (TF) antagonists, and uses in preventing or treating disorder associated with pathological TF function

INVENTOR(S): Stennicke, Henning Ralf; Petersen, Lars Christian; Bjorn, Soren E.

PATENT ASSIGNEE(S): Novo Nordisk A/S, Den.

SOURCE: PCT Int. Appl., 57 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004007557	A2	20040122	WO 2003-DK480	20030709
WO 2004007557	A3	20040422		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003242506	A1	20040202	AU 2003-242506	20030709
US 2004072755	A1	20040415	US 2003-617500	20030711
PRIORITY APPLN. INFO.:			DK 2002-1100	A 20020712
			US 2002-404567P	P 20020819
			WO 2003-DK480	W 20030709
AB	This invention relates to novel compds. which bind to tissue factor (TF) inhibiting TF-mediated FVIIa activity, and mediate a cytotoxic response. The present invention relates to conjugates of TF antagonists and a domain that act to elicit a cytotoxic response. In a first aspect, the present invention relates to a compound having the formula A-(LM)-C, wherein A is a TF antagonist; LM is an optional linker moiety; C comprises a cytotoxic domain, and wherein C or (LM)-C is conjugated at the glycosylation side chains of A, to a free sulfhydryl group present on A. Examples of TF antagonist includes inactivated FVIIa (FVIIai) and inhibitory antibodies against TF. The invention also relates to pharmaceutical compns. comprising the novel compds. as well as their use in the prophylaxis or treatment of disorders related to pathophysiol. TF functions including cancer, inflammation, atherosclerosis and ischemia/reperfusion.			
IC	ICM C07K019-00 ICS C07K016-36; C07K014-745; A61K038-36; A61K039-395; C07K007-06; C07K007-08; C07K014-00; A61K038-04; A61K038-16; A61K047-48			
CC	1-12 (Pharmacology)			
	Section cross-reference(s): 27, 63			
IT	Artery (coronary, bypass graft , (CABG); cytotoxic tissue factor (TF) antagonists, and uses in preventing or treating disorder associated with pathol. TF function)			
IT	184240-24-2D, polymer of, TF antagonist conjugates 184240-26-4D , TF antagonist conjugates RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (amino acid sequence, pro-apoptotic peptide; cytotoxic tissue factor (TF) antagonists, and uses in preventing or treating disorder associated with pathol. TF function)			
IT	184240-26-4D , TF antagonist conjugates RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (amino acid sequence, pro-apoptotic peptide; cytotoxic tissue factor (TF) antagonists, and uses in preventing or treating disorder associated with pathol. TF function)			
IT	184240-26-4D , TF antagonist conjugates RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic			

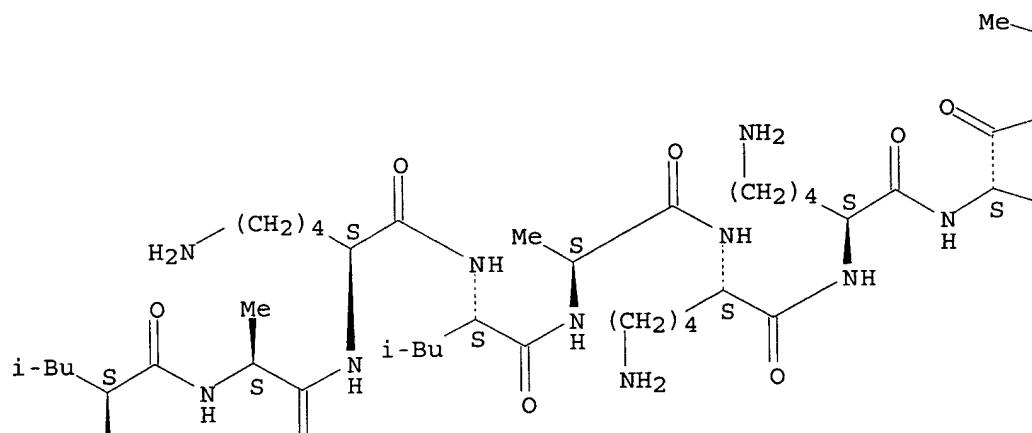
use); BIOL (Biological study); USES (Uses)
 (amino acid sequence, pro-apoptotic peptide; cytotoxic tissue factor
 (TF) antagonists, and uses in preventing or treating disorder associated
 with pathol. TF function)

RN 184240-26-4 HCAPLUS

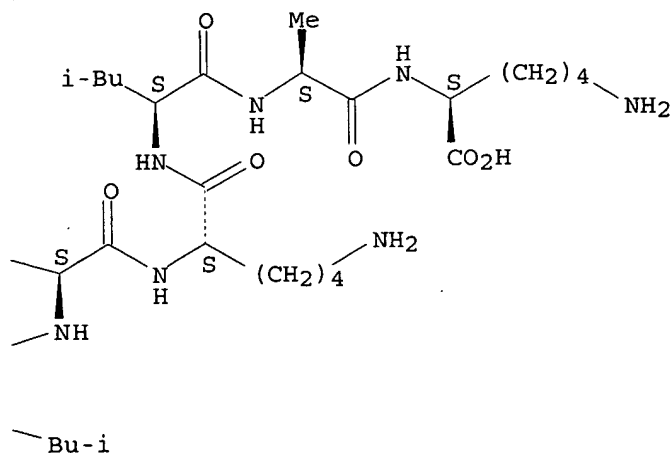
CN L-Lysine, L-lysyl-L-leucyl-L-alanyl-L-lysyl-L-leucyl-L-alanyl-L-lysyl-L-
 lysyl-L-leucyl-L-alanyl-L-lysyl-L-leucyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

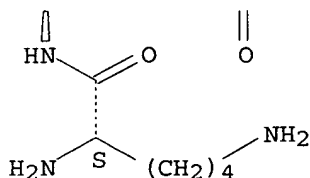
PAGE 1-A



PAGE 1-B



PAGE 2-A



L47 ANSWER 28 OF 43 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:51121 HCAPLUS

DOCUMENT NUMBER: 141:220941

TITLE: Pharmacokinetics and tumor retention of 125I-labeled RGD peptide are improved by PEGylation

AUTHOR(S): Chen, Xiaoyuan; Park, Ryan; Shahinian, Anthony H.; Bading, James R.; Conti, Peter S.

CORPORATE SOURCE: Department of Radiology, University of Southern California, Los Angeles, CA, 90033, USA

SOURCE: Nuclear Medicine and Biology (2004), 31(1), 11-19
CODEN: NMBIEO; ISSN: 0969-8051

PUBLISHER: Elsevier Science Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Tumor growth and metastasis are angiogenesis dependent. Overexpression of **integrin** $\alpha v \beta 3$ in angiogenic vessels as well as various malignant human tumors suggests the potential of suitably labeled antagonists of this adhesion receptor for radionuclide imaging and therapy of tumors. Small head-to-tail cyclic peptides including the Arg-Gly-Asp (RGD) amino acid sequence have been radiolabeled and studied in preclin. animal models. However, the fast blood clearance, high kidney and liver uptake, and rapid washout from tumors make this type of tracer ineffective for clin. applications. In this study we modified the cyclic pentapeptide c(RGDyK) with monofunctional methoxy-PEG (mPEG, M.W. = 2,000) and labeled the RGD-mPEG conjugate with 125I. We studied the tumor targeting efficacy and in vivo pharmacokinetic properties of 125I-RGD-mPEG by direct tissue sampling and autoradiog. in mice **xenografted** s.c. with U87MG glioblastoma. Compared to the 125I-RGD analog, this PEGylated RGD peptide revealed faster blood clearance, lower kidney uptake, and prolonged tumor uptake without compromising the receptor targeting ability.

CC 8-9 (Radiation Biochemistry)

Section cross-reference(s): 1, 63

ST glioblastoma angiogenesis antitumor RGD peptide PEGylation
integrin autoradiog biodistribution

IT Radiography

(autoradiography; pharmacokinetics and tumor retention of 125I-RGD in human U-87MG glioblastoma **xenografted** mouse was improved by PEGylation was studied using autoradiog. and direct tissue sampling)

IT Drug delivery systems

(carriers; 125I-RGD-PGD showed faster blood clearance, lower kidney uptake and prolonged tumor uptake without compromising receptor targeting ability than 125I-RGD in human U-87 MG glioblastoma **xenografted** mouse)

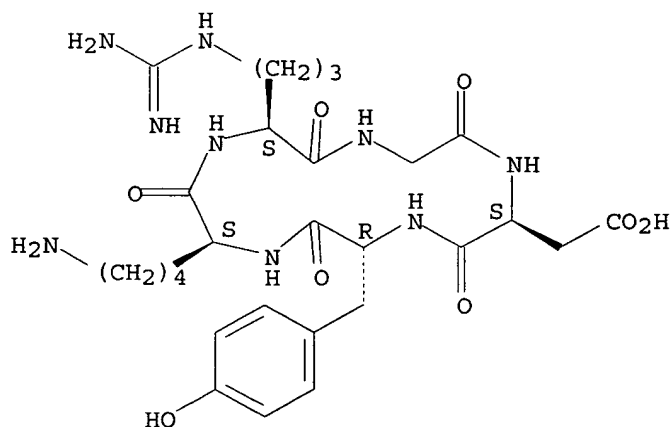
IT Peptides, biological studies

RL: PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(cyclic; 125I-RGD-PGD showed faster blood clearance, lower kidney uptake and prolonged tumor uptake without compromising receptor targeting ability than 125I-RGD in human U-87 MG glioblastoma **xenografted** mouse)

- IT Neuroglia, neoplasm
(glioblastoma; 125I-RGD-mPEG showed faster blood clearance, lower kidney uptake and prolonged tumor uptake without compromising receptor targeting ability than 125I-RGD in human U-87MG glioblastoma **xenografted** mouse)
- IT Drug targets
(**integrin** antagonist $\alpha v \beta 3$ 125I-RGD-mPEG showed faster blood clearance, lower kidney uptake and prolonged tumor uptake without compromising on receptor targeting than 125I-RGD in human U-87MG glioblastoma **xenografted** mouse)
- IT Scintigraphy
(pharmacokinetics and tumor retention of 125I-RGD in human U-87MG glioblastoma **xenografted** mouse was improved by PEGylation was studied using autoradiog. and direct tissue sampling)
- IT RGD peptides
RL: PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(pharmacokinetics and tumor retention of 125I-RGD in human U-87MG glioblastoma **xenografted** mouse was improved by PEGylation was studied using autoradiog. and direct tissue sampling)
- IT **Integrins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
($\alpha v \beta 3$; **integrin** antagonist $\alpha v \beta 3$ 125I-RGD-mPEG showed faster blood clearance, lower kidney uptake and prolonged tumor uptake without compromising on receptor targeting than 125I-RGD in human U-87MG glioblastoma **xenografted** mouse)
- IT **Integrins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
($\alpha \beta 3$; 125I-RGD-PGD showed faster blood clearance, lower kidney uptake and prolonged tumor uptake without compromising receptor targeting ability than 125I-RGD in human U-87 MG glioblastoma **xenografted** mouse)
- IT Polyoxyalkylenes, biological studies
RL: DGN (Diagnostic use); PKT (Pharmacokinetics); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(125I-RGD-PGD showed faster blood clearance, lower kidney uptake and prolonged tumor uptake without compromising receptor targeting ability than 125I-RGD in human U-87 MG glioblastoma **xenografted** mouse)
- IT Angiogenesis
Human
(125I-RGD-mPEG showed faster blood clearance, lower kidney uptake and prolonged tumor uptake without compromising receptor targeting ability than 125I-RGD in human U-87MG glioblastoma **xenografted** mouse)
- IT 14158-31-7DP, PEG-conjugated RGD peptide labeled with, biological studies
25322-68-3DP, 125I-labeled RGD peptide conjugate
RL: DGN (Diagnostic use); PKT (Pharmacokinetics); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(125I-RGD-PGD showed faster blood clearance, lower kidney uptake and prolonged tumor uptake without compromising receptor targeting ability than 125I-RGD in human U-87 MG glioblastoma **xenografted** mouse)
- IT 174569-25-6DP, 125I-labeled RGD cyclic peptide conjugate derivs.
RL: PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(125I-RGD-PGD showed faster blood clearance, lower kidney uptake and prolonged tumor uptake without compromising receptor targeting ability than 125I-RGD in human U-87 MG glioblastoma **xenografted** mouse)

- mouse)
- IT **217099-14-4**
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (125I-RGD-PGD showed faster blood clearance, lower kidney uptake and prolonged tumor uptake without compromising receptor targeting ability than 125I-RGD in human U-87 MG glioblastoma **xenografted** mouse)
- IT **217099-14-4DP**, 125I-labeled, polyethylene glycol conjugate derivs.
 RL: PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (125I-RGD-mPEG showed faster blood clearance, lower kidney uptake and prolonged tumor uptake without compromising receptor targeting ability than 125I-RGD in human U-87MG glioblastoma **xenografted** mouse)
- IT **217099-14-4**
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (125I-RGD-PGD showed faster blood clearance, lower kidney uptake and prolonged tumor uptake without compromising receptor targeting ability than 125I-RGD in human U-87 MG glioblastoma **xenografted** mouse)
- IT **217099-14-4DP**, 125I-labeled, polyethylene glycol conjugate derivs.
 RL: PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (125I-RGD-mPEG showed faster blood clearance, lower kidney uptake and prolonged tumor uptake without compromising receptor targeting ability than 125I-RGD in human U-87MG glioblastoma **xenografted** mouse)
- IT **217099-14-4**
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (125I-RGD-PGD showed faster blood clearance, lower kidney uptake and prolonged tumor uptake without compromising receptor targeting ability than 125I-RGD in human U-87 MG glioblastoma **xenografted** mouse)
- RN 217099-14-4 HCAPLUS
 CN Cyclo(L-arginylglycyl-L- α -aspartyl-D-tyrosyl-L-lysyl) (9CI) (CA INDEX NAME)

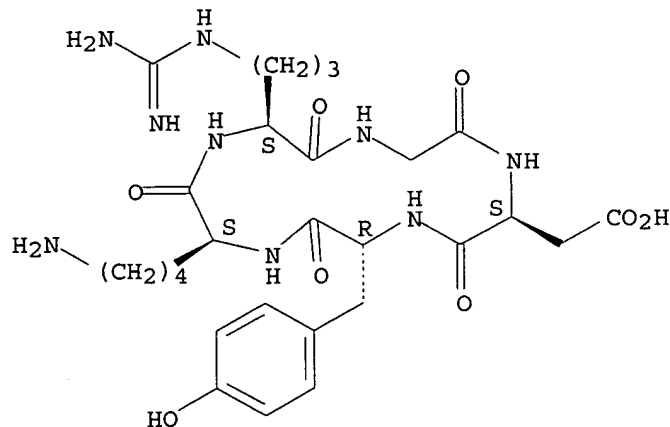
Absolute stereochemistry.



- IT **217099-14-4DP**, 125I-labeled, polyethylene glycol conjugate derivs.
 RL: PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (125I-RGD-mPEG showed faster blood clearance, lower kidney uptake and prolonged tumor uptake without compromising receptor targeting ability than 125I-RGD in human U-87MG glioblastoma **xenografted** mouse)

RN 217099-14-4 HCAPLUS
CN Cyclo(L-arginylglycyl-L- α -aspartyl-D-tyrosyl-L-lysyl) (9CI) (CA
INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 29 OF 43 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:836764 HCAPLUS
DOCUMENT NUMBER: 139:333095
TITLE: Colon tumor-specific binding peptides, and therapeutic
ad diagnostic uses thereof
INVENTOR(S): Kelly, Kimberly A.; Jones, David A.
PATENT ASSIGNEE(S): University of Utah Research Foundation, USA
SOURCE: PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003086284	A2	20031023	WO 2003-US10630	20030407
WO 2003086284	A3	20050909		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2481231	AA	20031023	CA 2003-2481231	20030407
AU 2003226299	A1	20031027	AU 2003-226299	20030407
EP 1575496	A2	20050921	EP 2003-746635	20030407
EP 1575496	A3	20051102		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				

US 2006058228 A1 20060316 US 2005-510155 20050711
 PRIORITY APPLN. INFO.: US 2002-369850P P 20020405
 WO 2003-US10630 W 20030407

OTHER SOURCE(S): MARPAT 139:333095

AB Phage display was used to screen peptide libraries that distinguish between well-differentiated (HCT116) and poorly-differentiated colon carcinoma cells (HT29). The screening protocol used selection and subtraction on intact, viable cells, resulting in phage libraries exhibiting high binding selectivity for the poorly-differentiated HT29 cells. A nine amino acid, disulfide-constrained peptide (RPM) was identified that selectively bound and was internalized into colon cancer cells. The peptide may be used to detect colon cancer cells and also may be used to selectively deliver therapeutic agents to the cells.

IC ICM A61K

CC 1-6 (Pharmacology)

Section cross-reference(s): 9

IT 615263-22-4D, peptide conjugates

RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (colon tumor-specific binding peptides, and therapeutic ad diagnostic uses)

IT 615263-22-4D, peptide conjugates

RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (colon tumor-specific binding peptides, and therapeutic ad diagnostic uses)

IT 615263-22-4D, peptide conjugates

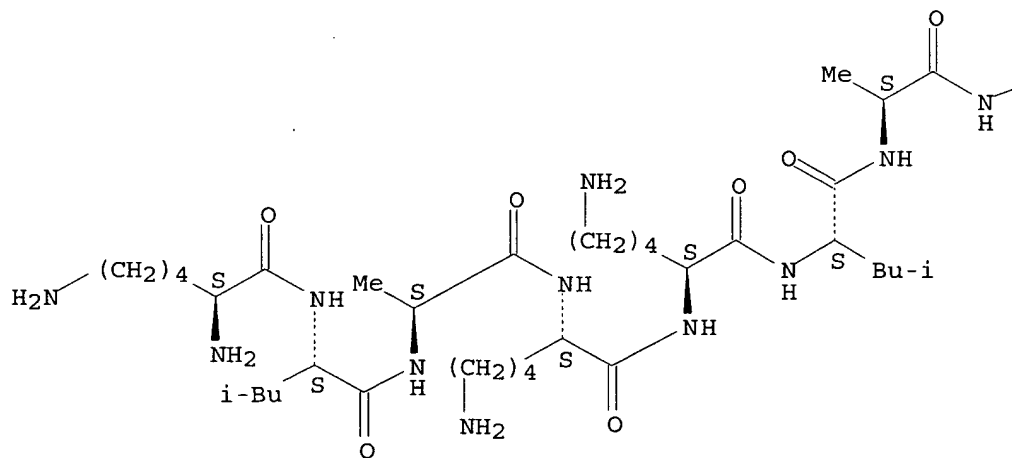
RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (colon tumor-specific binding peptides, and therapeutic ad diagnostic uses)

RN 615263-22-4 HCAPLUS

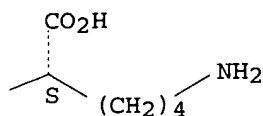
CN L-Lysine, L-lysyl-L-leucyl-L-alanyl-L-lysyl-L-lysyl-L-leucyl-L-alanyl-
 (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L47 ANSWER 30 OF 43 HCAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2003:408777 HCAPLUS
 DOCUMENT NUMBER: 139:7171
 TITLE: Preparation of vitronectin receptor antagonist
 pharmaceuticals for use in the diagnosis and treatment
 of cancer
 INVENTOR(S): Cheesman, Edward H.; Barrett, John A.; Carpenter, Alan
 P., Jr.; Rajopadhye, Milind; Sworin, Michael
 PATENT ASSIGNEE(S): Bristol-Myers Squibb Pharma Company, USA
 SOURCE: U.S., 86 pp., Cont.-in-part of U.S. Ser. No. 466,582.
 CODEN: USXXAM
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 7
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6569402	B1	20030527	US 2000-599365	20000621
US 6322770	B1	20011127	US 1999-281207	19990330
US 2002015680	A1	20020207	US 1999-281209	19990330
US 6524553	B2	20030225		
US 6548663	B1	20030415	US 1999-281050	19990330
US 6558649	B1	20030506	US 1999-466582	19991217
US 2003124120	A1	20030703	US 2002-269252	20021011
US 2003143235	A1	20030731	US 2002-306244	20021126
US 6818201	B2	20041116		
US 2003149262	A1	20030807	US 2002-306054	20021126
US 2004014964	A1	20040122	US 2003-348268	20030121
US 7090828	B2	20060815		
PRIORITY APPLN. INFO.:			US 1998-112831P	P 19981218
			US 1999-466582	A2 19991217
			US 1998-80150P	P 19980331
			US 1998-112715P	P 19981218
			US 1998-112732P	P 19981218
			US 1998-112829P	P 19981218
			US 1999-281050	A3 19990330
			US 1999-281209	A3 19990330
			US 2000-599365	A3 20000621

OTHER SOURCE(S): MARPAT 139:7171

AB The invention describes novel compds. (Q)d-Ln-Ch [Q is a residue having a 2-(carboxymethyl)-tetrahydro-1,4-benzodiazepine-type moiety; Ln is a linking group; Ch is a metal-bonding unit; d = 1-10] which are useful for the diagnosis and treatment of cancer and the imaging of tumors in a patient. The pharmaceuticals are comprised of a targeting moiety that binds to a receptor that is upregulated during angiogenesis, an optional linking group, and a therapeutically effective radioisotope or diagnostically effective imageable moiety. The imageable moiety is a gamma ray or positron emitting radioisotope, a magnetic resonance imaging contrast agent, an X-ray contrast agent, or an ultrasound contrast agent.

Thus, (S,S,S)-4-[N-[3-[3,6-diaza-10-[N-(benzimidazol-2-ylmethyl)-N-methylcarbamoyl]-5-(carboxymethyl)-4-oxobicyclo[5.4.0]undeca-1(7),8,10-trien-3-yl]propyl]carbamoyl]-4-[4-carboxy-2-[2-[1,4,7,10-tetraaza-4,7,10-tris(carboxymethyl)cyclodecyl]acetylaminobutanoylamino]butanoic acid (claimed compound) was prepared and used in the synthesis of ¹⁷⁷Lu, ⁹⁰Y and ¹¹¹In complexes.

IC ICM A61K005-00

ICS A61M036-14

INCL 424001650; 424001110; 424009100; 534014000

CC 34-3 (Amino Acids, Peptides, and Proteins)

Section cross-reference(s): 8, 28, 63, 78

IT 5704-04-1DP, Tricine, technetium-99 complexes 14133-76-7DP, Technetium 99, complexes with vitronectin receptor binding conjugates, preparation 63995-70-0DP, Tpppts, technetium-99 complexes 277327-56-7P 277327-58-9P 277327-59-0P 277327-61-4P 277327-62-5P 277327-64-7P 277328-27-5P 277328-39-9P 277328-42-4P 277328-43-5P 277328-45-7P 277328-46-8P 277328-47-9P 278180-25-9P 278180-26-0P 278180-27-1P 278180-28-2P 278180-29-3P 278180-30-6P 278180-31-7P 278180-32-8P 278180-36-2P 278180-38-4P 278180-40-8P 532983-26-9P 532983-27-0P 532983-28-1P 532983-29-2P 532983-30-5P

RL: DGN (Diagnostic use); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of peptidyl vitronectin receptor antagonist pharmaceuticals for diagnosis and treatment of cancer)

IT 50-07-7, Mitomycin 57-22-7, Vincristine 57-83-0, Progesterone, biological studies 59-05-2, Methotrexate 125-84-8, Aminoglutethimide 147-94-4, Cytarabine 302-79-4, Tretinoin 434-07-1, Oxymetholone 488-41-5, Mitobronitol 566-48-3, Formestane 2363-58-8, Epiteostanol 3094-09-5, Doxifluridine 3543-75-7, Bendamustin hydrochloride 3778-73-2, Ifosfamide 4291-63-8, Cladribine 4533-39-5, Nitracrine 4759-48-2, Isotretinoin 6620-60-6, Proglumide 9014-02-2, Zinostatin 9050-67-3, Sizofilan 10318-26-0, Mitolactol 10540-29-1, Tamoxifen 13311-84-7, Flutamide 13425-98-4, Improsulfan 14769-73-4, Levamisole 17902-23-7, Tegafur 18016-80-3, Lisuride 18883-66-4, Streptozocin 20830-81-3, Daunorubicin 21362-69-6, Mepitiostane 21416-67-1, Razoxane 22181-94-8, Butocin 22668-01-5 23214-92-8, Doxorubicin 24279-91-2, Carboquone 27314-97-2, 3-Amino-1,2,4-benzotriazine-1,4-dioxide 29069-24-7, Prednimustine 29767-20-2, Teniposide 33419-42-0, Etoposide 39325-01-4, Picibanil 41575-94-4, Carboplatin 42471-28-3, Nimustine 51264-14-3, Amsacrine 53643-48-4, Vindesine 53910-25-1, Pentostatin 54350-48-0, Etretnate 55726-47-1, Enocitabine 58337-35-2, Elliptinium acetate 61422-45-5, Carmofur 62304-98-7, Thymalfasin 70132-50-2 71486-22-1, Vinorelbine 74050-98-9, Ketanserin 81840-15-5, Vesnarinone 88876-88-4 90357-06-5, Bicalutamide 92118-27-9, Fotemustine 95058-81-4, Gemcitabine 95734-82-0, Nedaplatin 98631-95-9, Sobuzoxane 102676-47-1, Fadrozole 104958-90-9 108001-60-1 112809-51-5, Letrozole 112887-68-0, Raltitrexed 120287-85-6, Cetorelix

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(preparation of peptidyl vitronectin receptor antagonist pharmaceuticals for diagnosis and treatment of cancer)

IT 277328-46-8P

RL: DGN (Diagnostic use); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of peptidyl vitronectin receptor antagonist pharmaceuticals for diagnosis and treatment of cancer)

IT 277328-46-8P

RL: DGN (Diagnostic use); PAC (Pharmacological activity); SPN (Synthetic

preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

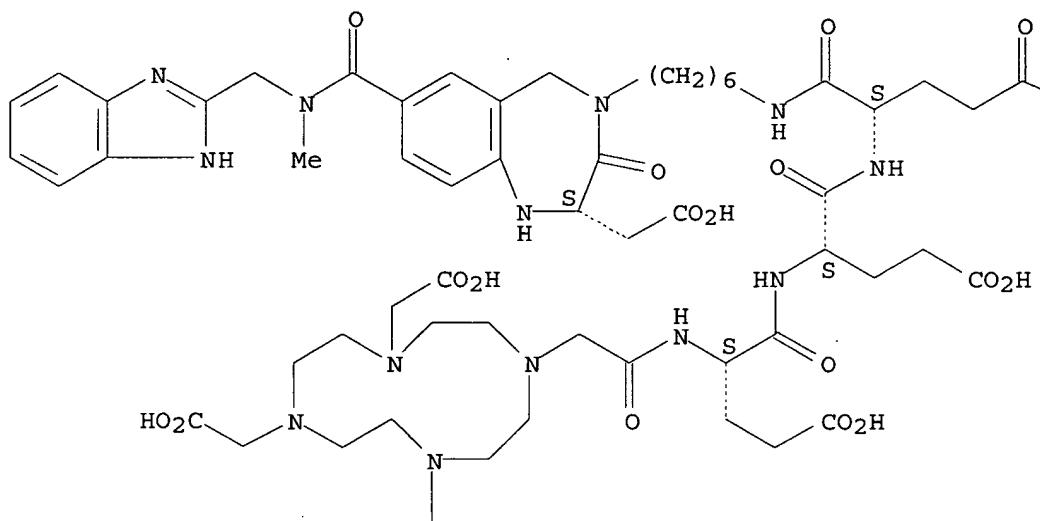
(preparation of peptidyl vitronectin receptor antagonist pharmaceuticals for diagnosis and treatment of cancer)

RN 277328-46-8 HCAPLUS

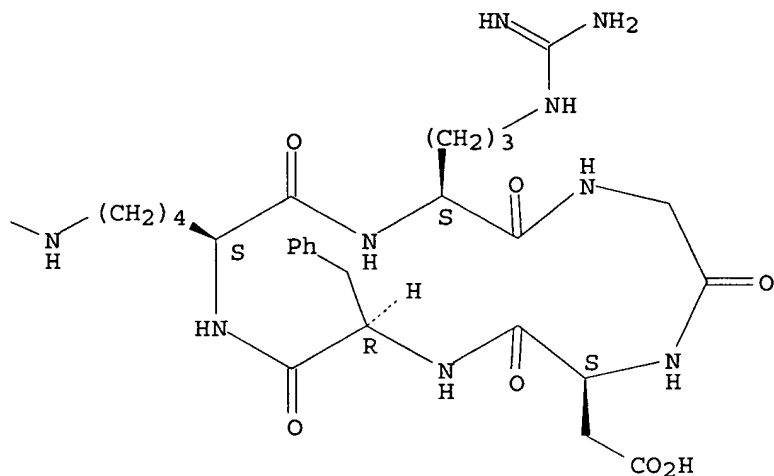
CN Cyclo[L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-N6-[N-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-L- α -glutamyl-L- α -glutamyl-N-[6-[(2S)-7-[[[1H-benzimidazol-2-ylmethyl)methylamino]carbonyl]-2-(carboxymethyl)-1,2,3,5-tetrahydro-3-oxo-4H-1,4-benzodiazepin-4-yl]hexyl]-L- α -glutaminyl]-L-lysyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.

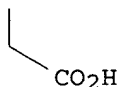
PAGE 1-A



PAGE 1-B



PAGE 2-A



REFERENCE COUNT: 162 THERE ARE 162 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 31 OF 43 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:235416 HCAPLUS

DOCUMENT NUMBER: 138:255514

TITLE: Pharmaceuticals for the imaging of angiogenic disorders for use in combination therapy

INVENTOR(S): Rajopadhye, Milind; Edwards, D. Scott; Barrett, John A.; Carpenter, Alan P., Jr.; Harris, Thomas D.; Heminway, Stuart J.; Liu, Shuang; Singh, Prahlad R.

PATENT ASSIGNEE(S): Bristol-Myers Squibb Pharma Company, USA

SOURCE: U.S., 86 pp., Cont.-in-part of U.S. Ser. No. 281,474. CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 7

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6537520	B1	20030325	US 2000-599295	20000621
US 6322770	B1	20011127	US 1999-281207	19990330
US 2002001566	A1	20020103	US 1999-281474	19990330
US 2002015680	A1	20020207	US 1999-281209	19990330
US 6524553	B2	20030225		
US 6548663	B1	20030415	US 1999-281050	19990330
ZA 2000004286	A	20010821	ZA 2000-4286	20000821
US 2003124120	A1	20030703	US 2002-269252	20021011
US 2003149262	A1	20030807	US 2002-306054	20021126

US 2003180305	A1	20030925	US 2003-342081	20030114
US 6800273	B2	20041005		
US 2006003926	A1	20060105	US 2003-622246	20030718
US 7052673	B2	20060530		

PRIORITY APPLN. INFO.:

US 1998-80150P	P	19980331
US 1998-112715P	P	19981218
US 1999-281474	A2	19990330
US 1998-112732P	P	19981218
US 1998-112829P	P	19981218
US 1998-112831P	P	19981218
US 1999-281050	A3	19990330
US 1999-281209	A3	19990330
US 2000-599295	A3	20000621
US 2003-342081	A3	20030114

OTHER SOURCE(S): MARPAT 138:255514

AB Compds. (Q)d-(Ln)m-Ch (Q is a peptide, d = 1-10, Ln is a linking group, m = 0-1, Ch is a metal-bonding unit) were prepared for use in the diagnosis and treatment of cancer in combination therapy in a patient. The present invention also provides novel compds. useful for monitoring therapeutic angiogenesis treatment and destruction of new angiogenic vasculature. The pharmaceuticals are comprised of a targeting moiety that binds to a receptor that is upregulated during angiogenesis, an optional linking group, and a therapeutically effective radioisotope or diagnostically effective imageable moiety. Thus, cyclo{Arg-Gly-Asp-D-Tyr(N-[2-[[[5-[carbonyl]-2-pyridinyl]hydrazono]methyl]benzenesulfonic acid]-3-aminopropyl)-Val} was prepared by acylation of cyclo{Arg-Gly-Asp-D-Tyr(3-aminopropyl)-Val} with 2-[[[5-[[2,5-dioxo-1-pyrrolidinyl]oxy]carbonyl]-2-pyridinyl]hydrazono]methyl]benzenesulfonic acid monosodium salt and converted into radiopharmaceutical ^{99m}Tc(VnA) (tricine) (phosphine), where VnA represents the vitronectin receptor antagonist.

IC ICM A61K051-00

ICS A61M036-14

INCL 424001690; 424001110; 424001650; 424009100; 534014000

CC 34-3 (Amino Acids, Peptides, and Proteins)

Section cross-reference(s): 8, 63, 78

IT **Integrins**

RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (αvβ3, disease associated with; preparation of peptide derivs. for the imaging of angiogenic disorders and the treatment of cancer in combination therapy)

IT 50-07-7, Mitomycin 57-22-7, Vincristine 57-83-0, Progesterone, biological studies 59-05-2, Methotrexate 125-84-8, Aminogluthethimide 147-94-4, Cytarabine 302-79-4, Tretinoin 434-07-1, Oxymetholone 488-41-5, Mitobronitol 566-48-3, Formestane 2363-58-8, Epitiostanol 3094-09-5, Doxifluridine 3778-73-2, Ifosfamide 4291-63-8, Cladribine 4533-39-5, Nitracrine 4759-48-2, Isotretinoin 6620-60-6, Proglumide 9014-02-2, Zinostatin 9034-40-6, Lhrf 9050-67-3, Sizofilan 10318-26-0, Mitolactol 10540-29-1, Tamoxifen 13311-84-7, Flutamide 13425-98-4, Improsulfan 14769-73-4, Levamisole 17902-23-7, Tegafur 18016-80-3, Lisuride 18883-66-4, Streptozocin 20830-81-3, Daunorubicin 21362-69-6, Mepitiostane 21416-67-1, Razoxane 22181-94-8, Butocin 23214-92-8, **Doxorubicin** 24279-91-2, Carboquone 29069-24-7, Prednimustine 29767-20-2, Teniposide 33419-42-0, Etoposide 39325-01-4, Picibanil 41575-94-4, Carboplatin 42471-28-3, Nimustine 51264-14-3, Amsacrine 53643-48-4, Vindesine 53910-25-1, Pentostatin 54350-48-0, Etrretinate 55726-47-1, Enocitabine 58337-35-2, Elliptinium acetate 61422-45-5, Carmofur 62304-98-7, Thymalfasin 71486-22-1, Vinorelbine 74050-98-9, Ketanserin 81627-83-0, Colony stimulating factor-1 81840-15-5, Vesnarinone 83869-56-1, Colony stimulating

factor-2 90357-06-5, Bicalutamide 92118-27-9, Fotemustine
 95058-81-4, Gemcitabine 95734-82-0, Nedaplatin 98631-95-9, Sobuzoxane
 102676-47-1, Fadrozole 104958-90-9 108001-60-1 112809-51-5,
 Letrozole 112887-68-0, Raltitrexed 120287-85-6, Cetorelix
 173146-27-5, Denileukin diftitox

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (anticancer agents as adjuvants in the treatment of cancer with peptide
 derivs. and their radioactive metal complexes)

IT 202930-91-4P 250611-72-4P 250611-73-5P 250611-74-6P
 250611-75-7P 250611-76-8P 250611-77-9P 250611-78-0P
 250611-79-1P 250611-80-4P 250611-81-5P
 250611-82-6P 250611-83-7P 250611-84-8P
 250611-85-9P 250611-86-0P 250611-87-1P 250611-88-2P
 250611-89-3P 250611-90-6P 250611-91-7P 250611-92-8P 250611-93-9P
 250611-94-0P 250611-95-1P 250611-96-2P 250611-97-3P 250611-98-4P
 250611-99-5P 250612-00-1P 250612-01-2P 250612-02-3P 250612-03-4P
 250612-04-5P 250612-05-6P 250612-06-7P 250612-07-8P
 250612-08-9P 250612-09-0P 250612-10-3P 250612-11-4P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic
 preparation); THU (Therapeutic use); BIOL (Biological study); PREP
 (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of peptide derivs. for the imaging of angiogenic disorders and
 the treatment of cancer in combination therapy)

IT 250611-72-4DP, technetium-99m tricine triazole complex 250612-12-5P
 250612-13-6P 250612-14-7P 250612-15-8P 250612-16-9P 250612-17-0P
 250612-18-1P 250612-19-2P 250612-20-5P 250612-21-6P 250612-22-7P
 250612-24-9P 250612-25-0P 250612-26-1P
 250614-19-8P 250614-20-1P 250614-21-2P 250614-22-3P
 250614-23-4P 250614-24-5P 250614-25-6P
 250614-26-7P 250614-27-8P 250614-28-9P 250614-29-0P 250614-30-3P
 250614-31-4P 250614-32-5P 250614-33-6P 250614-34-7P 250614-35-8P
 250614-36-9P 250614-37-0P 250614-38-1P 250614-39-2P
 250614-41-6P 250614-42-7P 250614-43-8P
 250614-44-9P 250614-45-0P 250614-46-1P
 250614-47-2P 250614-48-3P 851024-71-0P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
 (Uses)

(preparation of peptide derivs. for the imaging of angiogenic disorders and
 the treatment of cancer in combination therapy)

IT 108-30-5, reactions 288-88-0, 1H-1,2,4-Triazole 5437-45-6, Benzyl
 bromoacetate 5704-04-1, Tricine 23911-26-4,
 Diethylenetriaminepentaacetic dianhydride 63995-70-0, Tppts
 63995-75-5, TPPMS 64018-22-0, TPPDS 122555-91-3 161552-03-0
 180468-25-1 186305-11-3 194920-62-2 250612-83-0D, resin-bound
 250612-84-1D, resin-bound 250612-85-2D, resin-bound 250612-86-3
 250612-87-4 250612-88-5D, resin-bound 250612-89-6D, resin-bound
 250612-90-9D, resin-bound 250612-92-1D, resin-bound 250612-93-2D,
 resin-bound 250612-94-3

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of peptide derivs. for the imaging of angiogenic disorders and
 the treatment of cancer in combination therapy)

IT 137076-54-1P 192635-89-5P 246234-73-1P 250612-28-3P 250612-30-7P
 250612-31-8P 250612-32-9P 250612-34-1P 250612-36-3P 250612-38-5P
 250612-40-9P 250612-41-0P 250612-42-1P
 250612-43-2P 250612-44-3P 250612-46-5P
 250612-48-7P 250612-50-1P 250612-51-2P 250612-52-3P
 250612-54-5P 250612-56-7P 250612-57-8P 250612-59-0P 250612-61-4P
 250612-62-5P 250612-64-7P 250612-65-8P 250612-67-0P 250612-69-2P
 250612-71-6P 250612-72-7P 250612-74-9P 250612-75-0P 250612-77-2P

250612-78-3P 250612-80-7P 250612-82-9P 250636-75-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of peptide derivs. for the imaging of angiogenic disorders and the treatment of cancer in combination therapy)

IT 202930-91-4P 250611-78-0P 250611-79-1P
250611-80-4P 250611-81-5P 250611-82-6P
250611-83-7P 250611-84-8P 250611-85-9P
250612-06-7P 250612-07-8P 250612-08-9P
250612-09-0P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of peptide derivs. for the imaging of angiogenic disorders and the treatment of cancer in combination therapy)

IT 250612-24-9P 250612-25-0P 250612-26-1P
250614-22-3P 250614-23-4P 250614-24-5P
250614-25-6P 250614-38-1P 250614-39-2P
250614-41-6P 250614-42-7P 250614-43-8P
250614-44-9P 250614-46-1P 250614-47-2P
851024-71-0P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of peptide derivs. for the imaging of angiogenic disorders and the treatment of cancer in combination therapy)

IT 161552-03-0

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of peptide derivs. for the imaging of angiogenic disorders and the treatment of cancer in combination therapy)

IT 250612-41-0P 250612-42-1P 250612-43-2P
250612-44-3P 250612-46-5P 250612-48-7P
250612-50-1P 250612-82-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of peptide derivs. for the imaging of angiogenic disorders and the treatment of cancer in combination therapy)

IT 202930-91-4P 250611-78-0P 250611-79-1P
250611-80-4P 250611-81-5P 250611-82-6P
250611-83-7P 250611-84-8P 250611-85-9P
250612-06-7P 250612-07-8P 250612-08-9P
250612-09-0P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

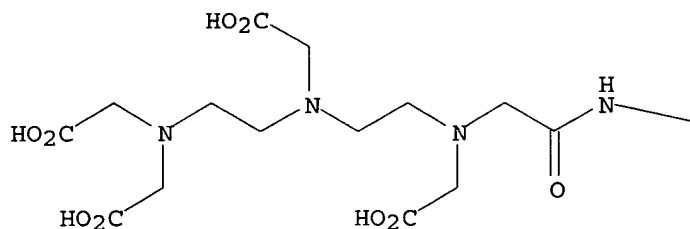
(preparation of peptide derivs. for the imaging of angiogenic disorders and the treatment of cancer in combination therapy)

RN 202930-91-4 HCAPLUS

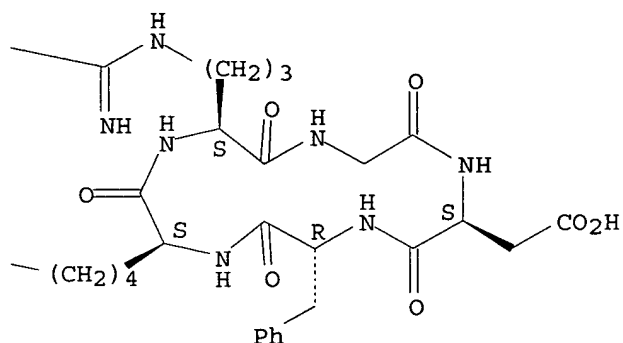
CN Cyclo[L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-N⁶-[N-[2-[[2-[bis(carboxymethyl)amino]ethyl](carboxymethyl)amino]ethyl]-N-(carboxymethyl)glycyl]-L-lysyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

H₂N—

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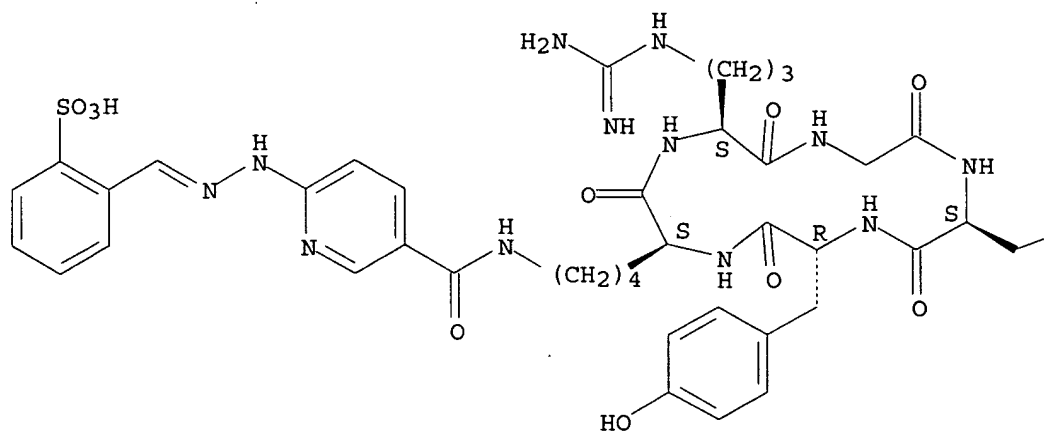


RN 250611-78-0 HCAPLUS

CN Cyclo[L-arginylglycyl-L- α -aspartyl-D-tyrosyl-N6-[[6-[[2-sulfophenyl)methylene]hydrazino]-3-pyridinyl]carbonyl]-L-lysyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

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PAGE 1-B

—CO₂H

RN 250611-79-1 HCAPLUS

CN Cyclo[L-arginylglycyl-L-α-aspartyl-D-tyrosyl-N6-[[6-[[2-sulfophenyl)methylene]hydrazino]-3-pyridinyl]carbonyl]-L-lysyl],
mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

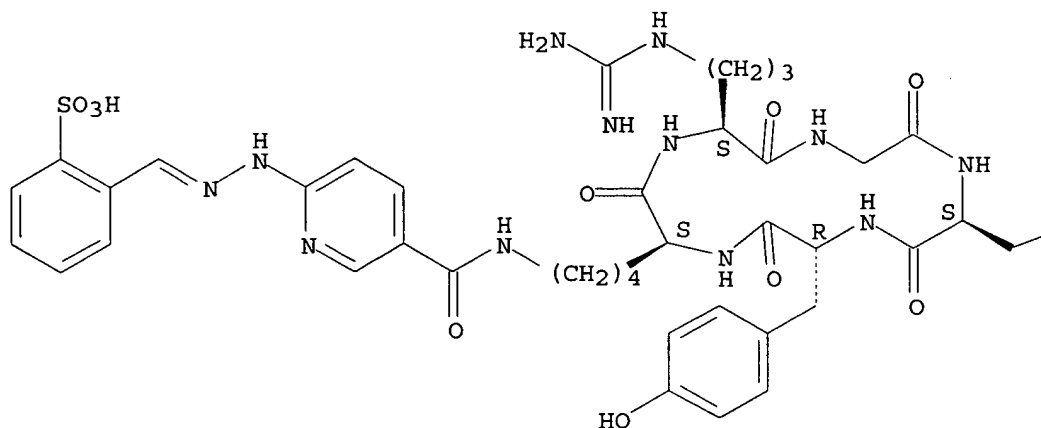
CM 1

CRN 250611-78-0

CMF C40 H50 N12 O12 S

Absolute stereochemistry.
Double bond geometry unknown.

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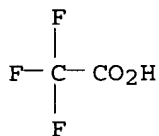
PAGE 1-B

—CO₂H

CM 2

CRN 76-05-1

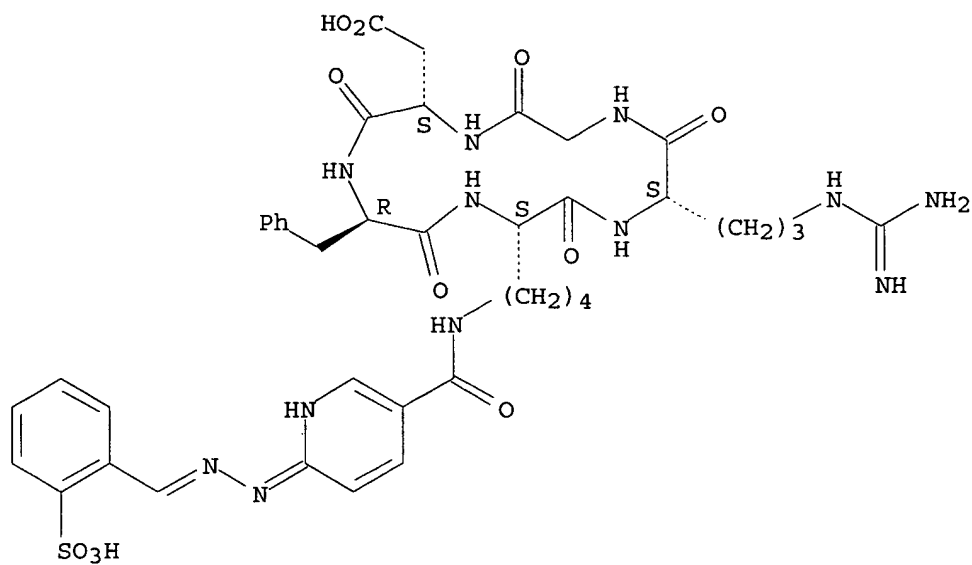
CMF C2 H F3 O2



RN 250611-80-4 HCAPLUS

CN Cyclo[L-arginylglycyl-L-α-aspartyl-D-phenylalanyl-N6-[[6-[[[(2-sulfophenyl)methylene]hydrazino]-3-pyridinyl]carbonyl]-L-lysyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



RN 250611-81-5 HCAPLUS

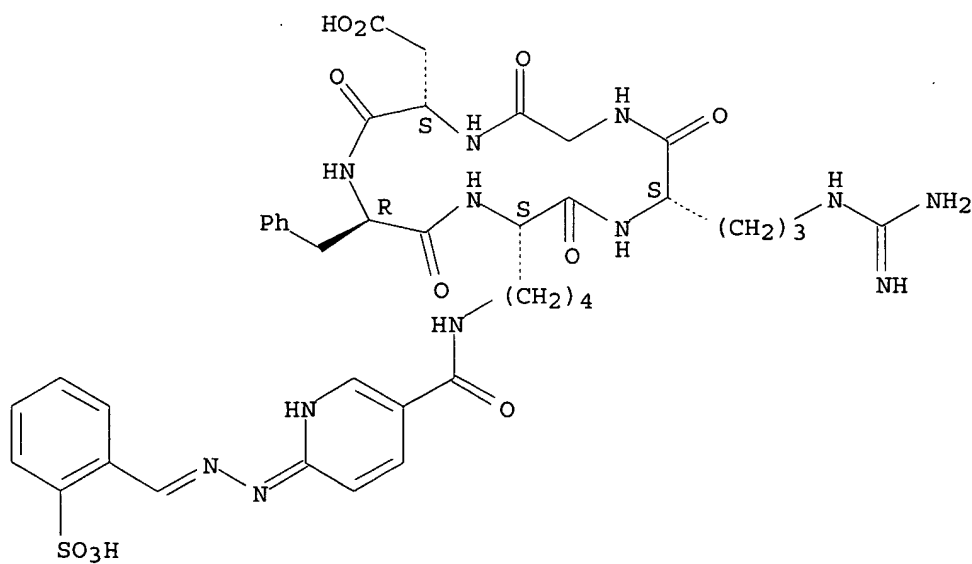
CN Cyclo[L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-N6-[[6-[[[(2-sulfophenyl)methylene]hydrazino]-3-pyridinyl]carbonyl]-L-lysyl], mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 250611-80-4

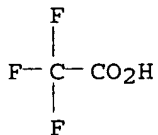
CMF C40 H50 N12 O11 S

Absolute stereochemistry.
Double bond geometry unknown.



CM 2

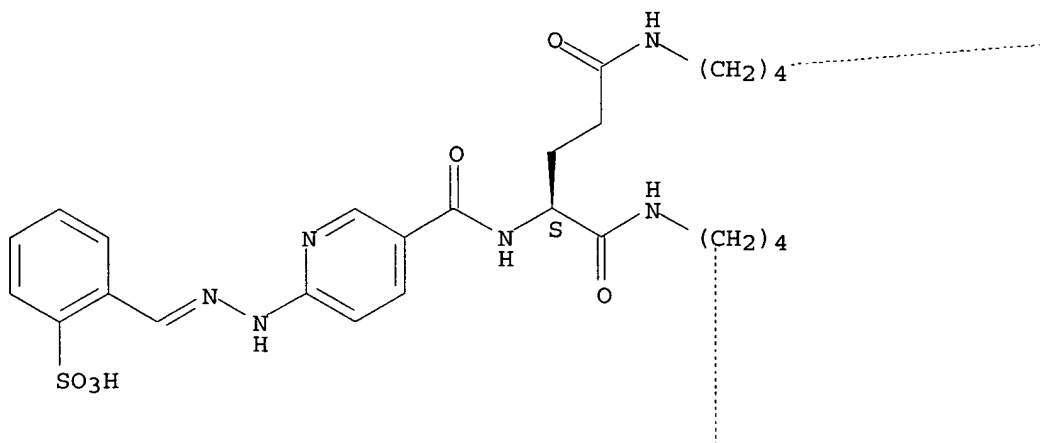
CRN 76-05-1
CMF C2 H F3 O2



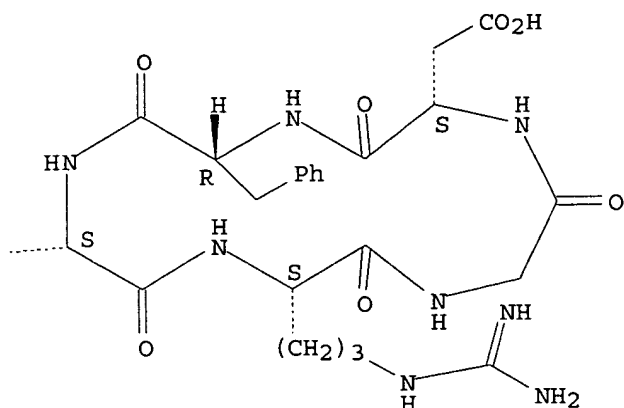
RN 250611-82-6 HCAPLUS
CN Cyclo(L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-L-lysyl),
5,5'-[N-[[6-[[[(2-sulfophenyl)methylene]hydrazino]-3-pyridinyl]carbonyl]-L-
glutamoyl]bis- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

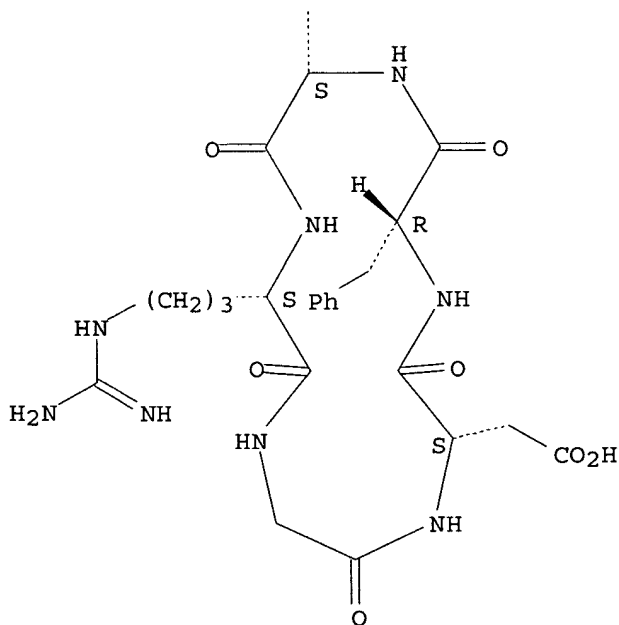
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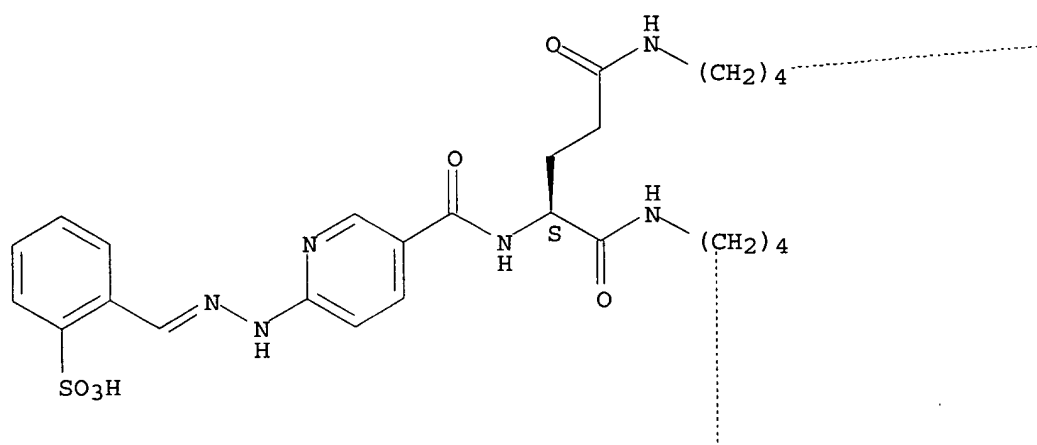
RN 250611-83-7 HCAPLUS
 CN Cyclo(L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-L-lysyl),
 5,5'-[N-[[6-[[[(2-sulfophenyl)methylene]hydrazino]-3-pyridinyl]carbonyl]-L-
 glutamoyl]bis-, bis(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

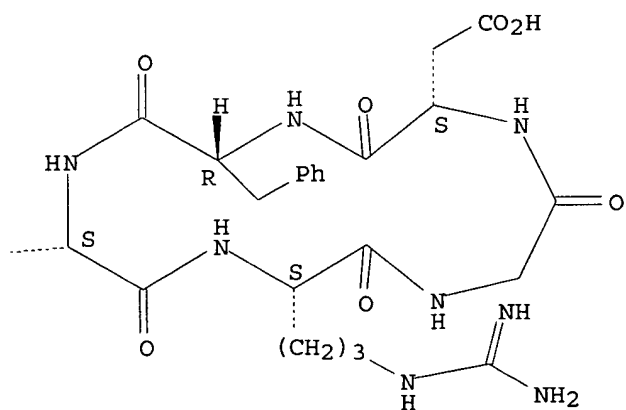
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 CMF C72 H96 N22 O20 S

Absolute stereochemistry.
 Double bond geometry unknown.

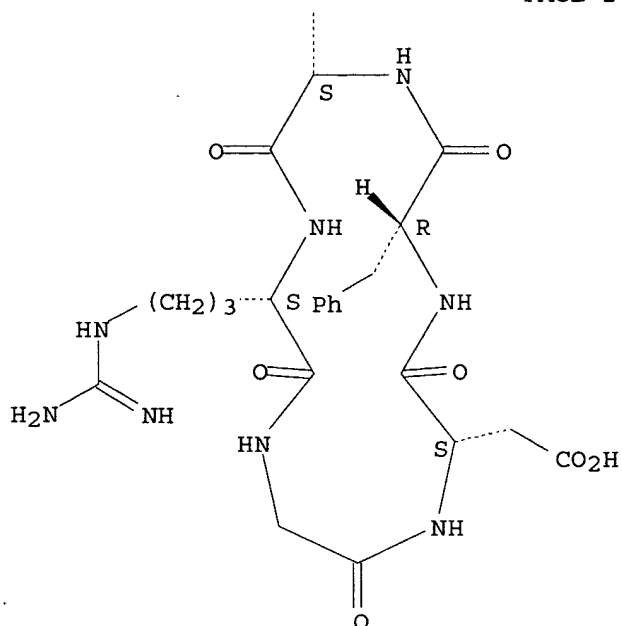
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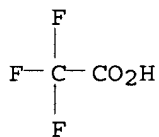
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CM 2

CRN 76-05-1

CMF C2 H F3 O2



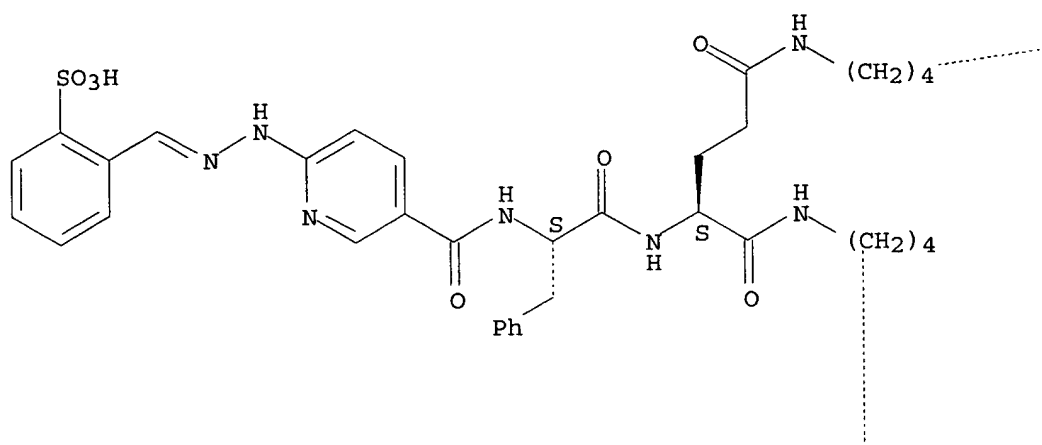
RN 250611-84-8 HCAPLUS

CN Cyclo(L-arginylglycyl-L-α-aspartyl-D-phenylalanyl-L-lysyl),
5,5'-[N-[[6-[[[(2-sulfophenyl)methylene]hydrazino]-3-pyridinyl]carbonyl]-L-phenylalanyl-L-glutamoyl]bis- (9CI) (CA INDEX NAME)

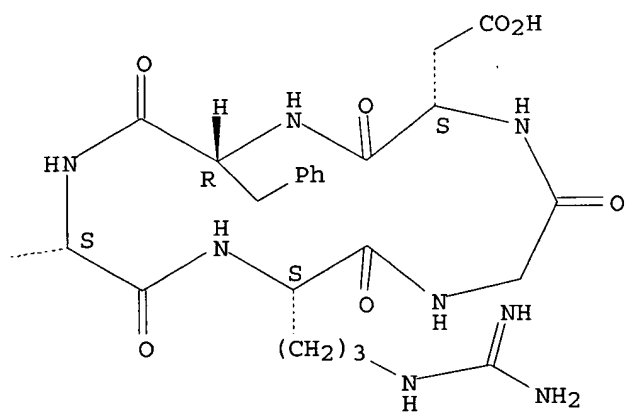
Absolute stereochemistry.

Double bond geometry unknown.

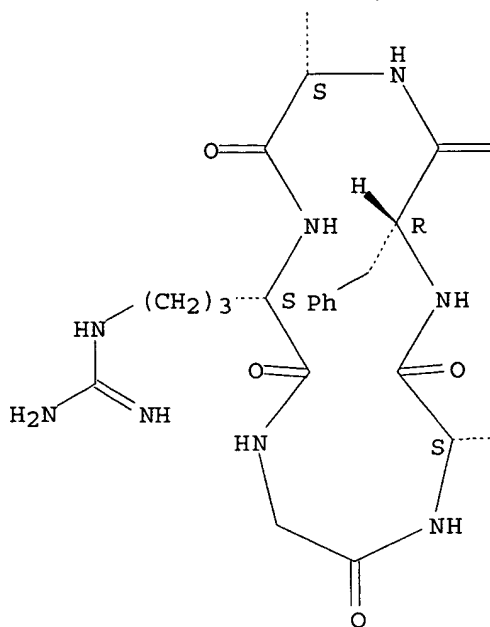
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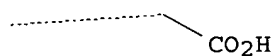
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RN 250611-85-9 HCAPLUS
 CN Cyclo(L-arginylglycyl-L-α-aspartyl-D-phenylalanyl-L-lysyl),
 5,5'-[N-[[6-[[[(2-sulfophenyl)methylene]hydrazino]-3-pyridinyl]carbonyl]-L-
 phenylalanyl-L-glutamoyl]bis-, bis(trifluoroacetate) (9CI) (CA INDEX
 NAME)

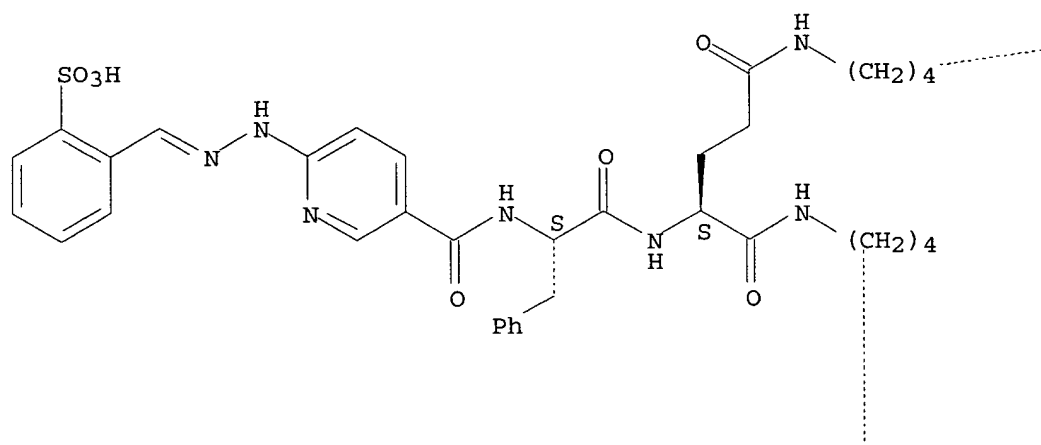
CM 1

CRN 250611-84-8
 CMF C81 H105 N23 O21 S

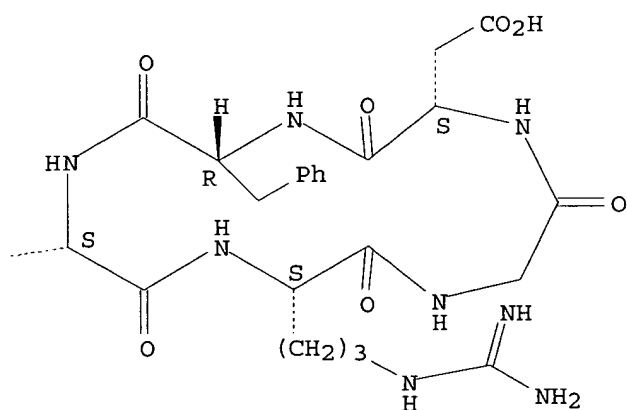
Absolute stereochemistry.

Double bond geometry unknown..

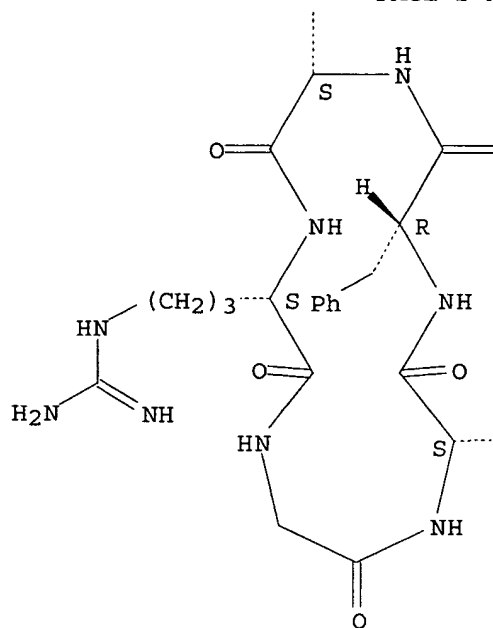
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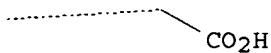
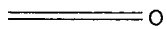
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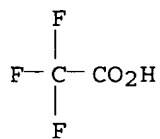
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CM 2

CRN 76-05-1

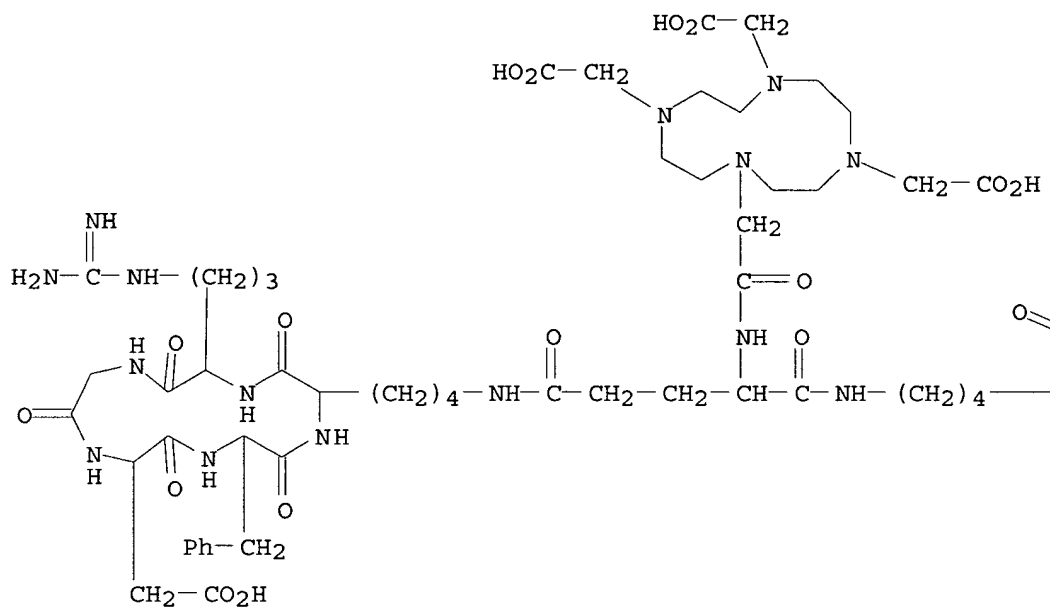
CMF C2 H F3 O2



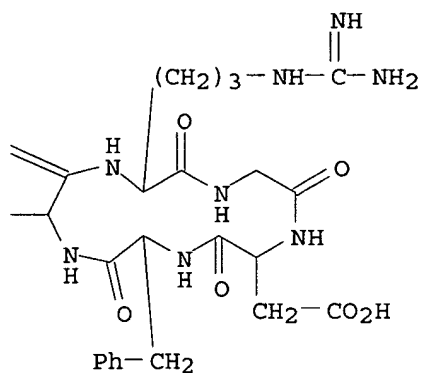
RN 250612-06-7 HCAPLUS

CN Cyclo(L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-L-lysyl),
 5,5'-[N-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-L-glutamoyl]bis- (9CI) (CA INDEX NAME)

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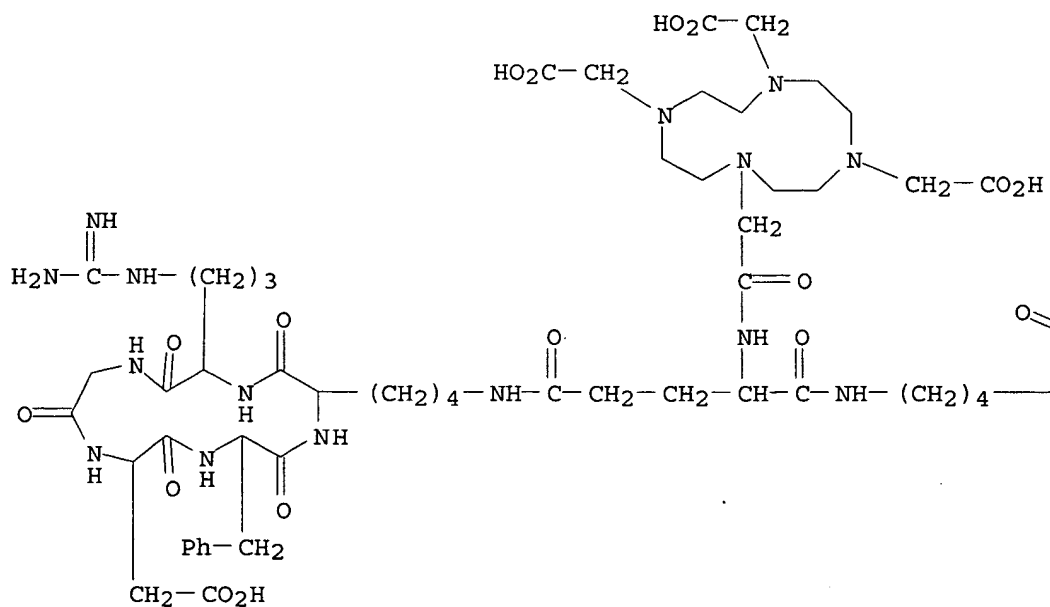
RN 250612-07-8 HCAPLUS
 CN Cyclo(L-arginylglycyl-L-α-aspartyl-D-phenylalanyl-L-lysyl),
 5,5'-[N-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-L-glutamoyl]bis-, bis(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

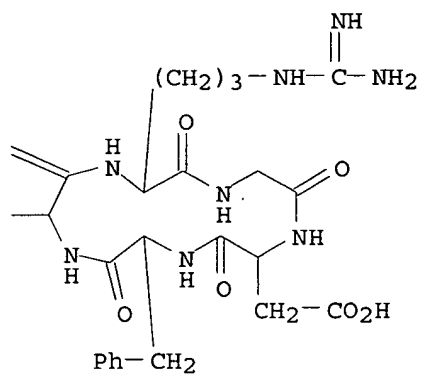
CRN 250612-06-7

CMF C75 H113 N23 O23

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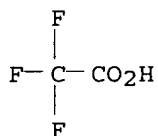
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CM 2

CRN 76-05-1

CMF C2 H F3 O2



RN 250612-08-9 HCAPLUS

CN Cyclo[L-arginylglycyl-L-α-aspartyl-D-phenylalanyl-N6-[N-[2-[[2-[bis(carboxymethyl)amino]ethyl](carboxymethyl)amino]ethyl]-N-(carboxymethyl)glycyl]-L-lysyl], mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

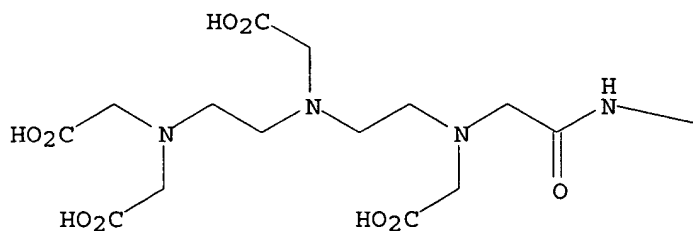
CRN 202930-91-4

CMF C41 H62 N12 O16

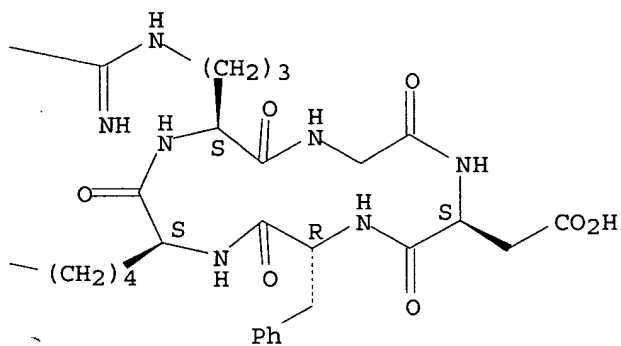
Absolute stereochemistry.

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H₂N—



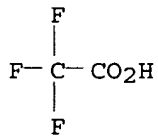
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CM 2

CRN 76-05-1

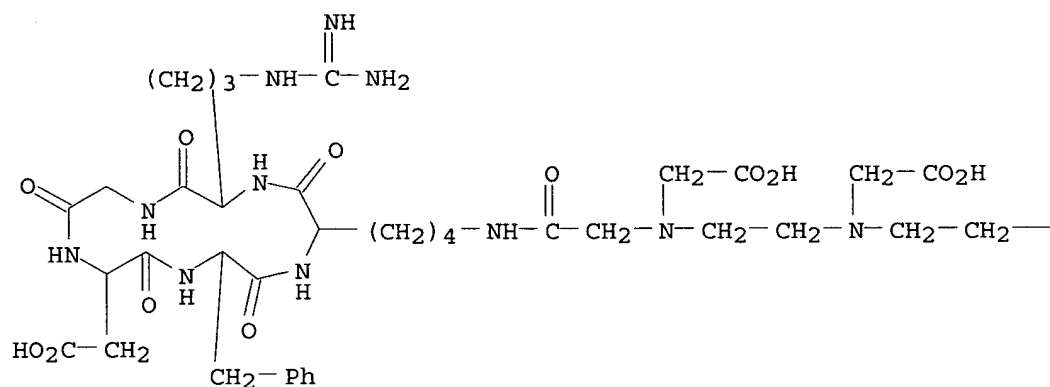
CMF C2 H F3 O2



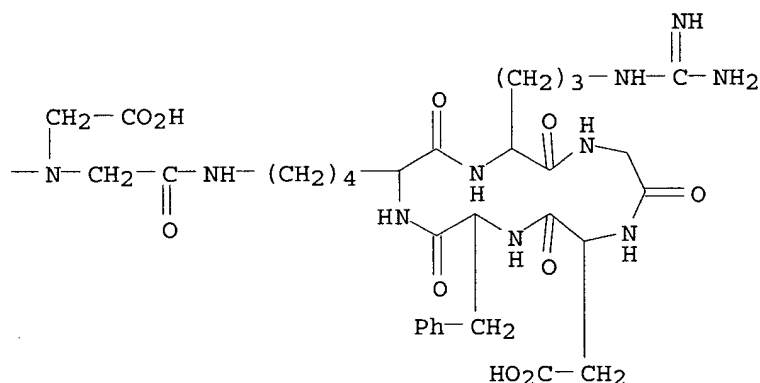
RN 250612-09-0 HCAPLUS

CN Cyclo[L-arginylglycyl-L-α-aspartyl-D-phenylalanyl-N6-[N-(carboxymethyl)glycyl]-L-lysyl], 1',1'''-[[[(carboxymethyl)imino]di-2,1-ethanediyl]bis-(9CI) (CA INDEX NAME)

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IT 250612-24-9P 250612-25-0P 250612-26-1P
 250614-22-3P 250614-23-4P 250614-24-5P
 250614-25-6P 250614-38-1P 250614-39-2P
 250614-41-6P 250614-42-7P 250614-43-8P
 250614-44-9P 250614-46-1P 250614-47-2P
 851024-71-0P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
 (Uses)

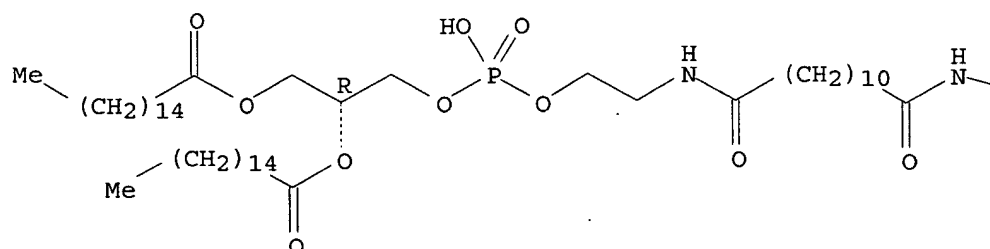
(preparation of peptide derivs. for the imaging of angiogenic disorders and
 the treatment of cancer in combination therapy)

RN 250612-24-9 HCAPLUS

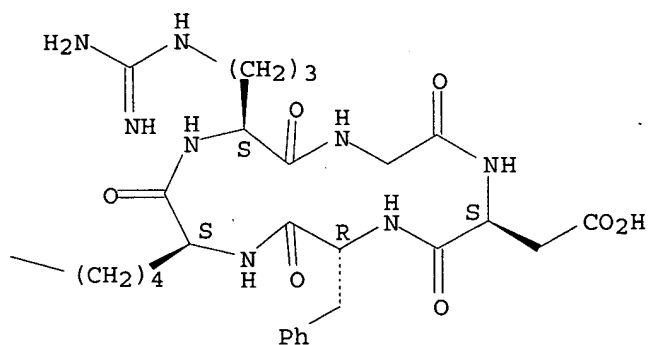
CN Cyclo[L-arginylglycyl-L-α-aspartyl-D-phenylalanyl-N6-[(20R)-17-
 hydroxy-17-oxido-1,12,23-trioxo-20-[(1-oxohexadecyl)oxy]-16,18,22-trioxa-
 13-aza-17-phosphaoctatriacont-1-yl]-L-lysyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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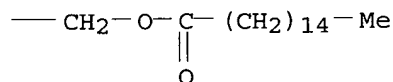
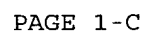
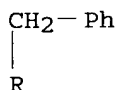


PAGE 1-B

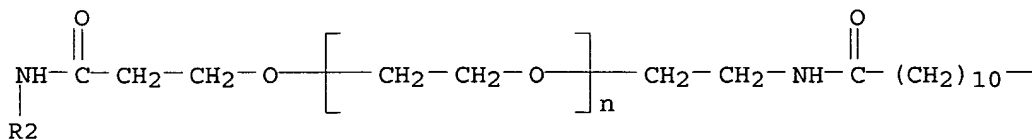


RN 250612-25-0 HCAPLUS
 CN Cyclo[L-arginylglycyl-L-α-aspartyl-D-phenylalanyl-N6-(3-hydroxy-1-oxopropyl)-L-lysyl], ether with α-[(23R)-20-hydroxy-20-oxido-4,15,26-trioxo-23-[(1-oxohexadecyl)oxy]-19,21,25-trioxa-3,16-diaza-20-phosphahentriacont-1-yl]-ω-hydroxypoly(oxy-1,2-ethanediyl) (9CI)
 (CA INDEX NAME)

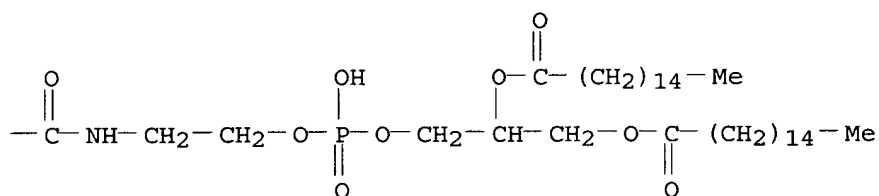
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RN	250612-26-1	HCAPLUS
CN	Cyclo(L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-L-lysyl), 5,5'-[N-(3-hydroxy-1-oxopropyl)-L-glutamoyl]bis-, ether with α -[(23R)-20-hydroxy-20-oxido-4,15,26-trioxo-23-[(1-oxohexadecyl)oxy]- 19,21,25-trioxa-3,16-diaza-20-phosphahentriacont-1-yl]- ω - hydroxypoly(oxy-1,2-ethanediyl) (9CI) (CA INDEX NAME)	

[illegible]O=C(NC(=O)N(Cc1ccccc1)C(=O)NC(=O)CC(=O)N(R)C(=O)N)C
$$\begin{array}{c} \text{NH} \\ || \\ (\text{CH}_2)_3 - \text{NH} - \text{C} - \text{NH}_2 \\ | \\ \text{R} \end{array}$$


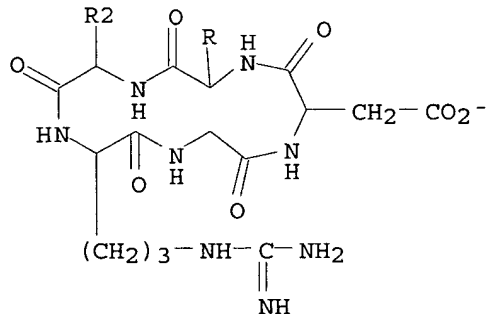
PAGE 2-B



RN 250614-22-3 HCAPLUS

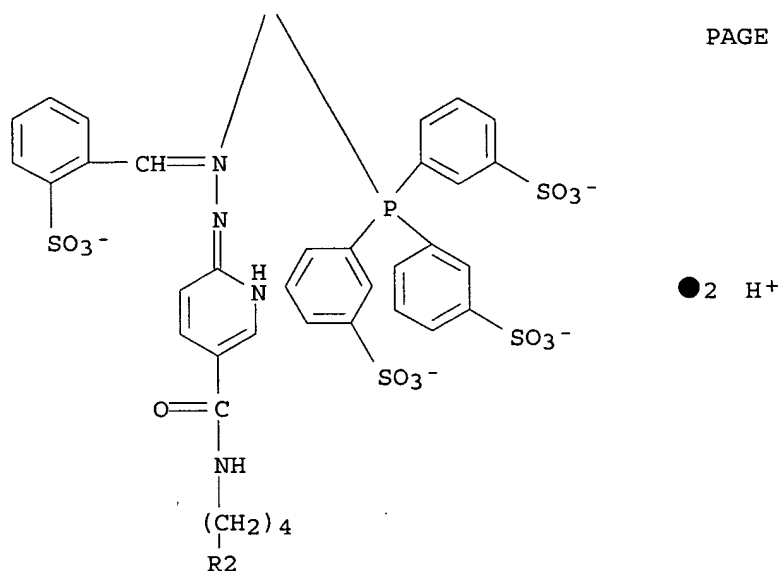
CN Technetate(5-)-99Tc, [cyclo[L-arginylglycyl-L- α -aspartyl-D-tyrosyl-N6-[[6-[[[(2-sulfophenyl)methylene]hydrazino- κ N2]-3-pyridinyl]carbonyl]-L-lysylato(2-)]][N-[2-hydroxy-1,1-bis[(hydroxy- κ O)methyl]ethyl]glycinato(3-)- κ N, κ O][[3,3',3''-(phosphinidyne- κ P)tris[benzenesulfonato]](3-)]-, trisodium dihydrogen (9CI) (CA INDEX NAME)

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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

PAGE 3-A

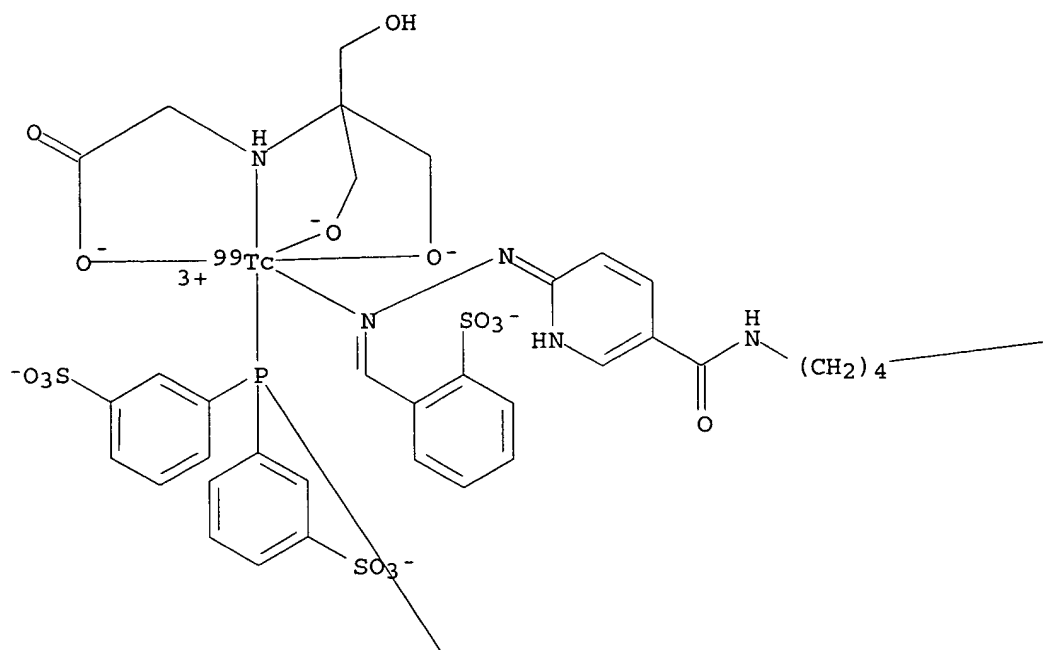


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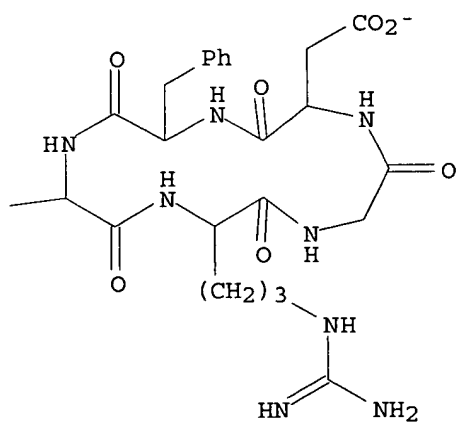
● 3 Na⁺

RN 250614-23-4 HCAPLUS
 CN Technetate(5-) -99Tc, [cyclo[L-arginylglycyl-L-α-aspartyl-D-phenylalanyl-N6-[[6-[[[(2-sulfophenyl)methylene]hydrazino-κN2]-3-pyridinyl]carbonyl]-L-lysylato(2-)]] [N-[2-hydroxy-1,1-bis[(hydroxy-κO)methyl]ethyl]glycinato(3-)-κN,κO] [[3,3',3''-(phosphinidyne-κP)tris[benzenesulfonato]](3-)]-, trisodium dihydrogen (9CI) (CA INDEX NAME)

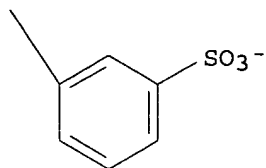
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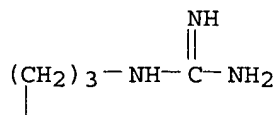
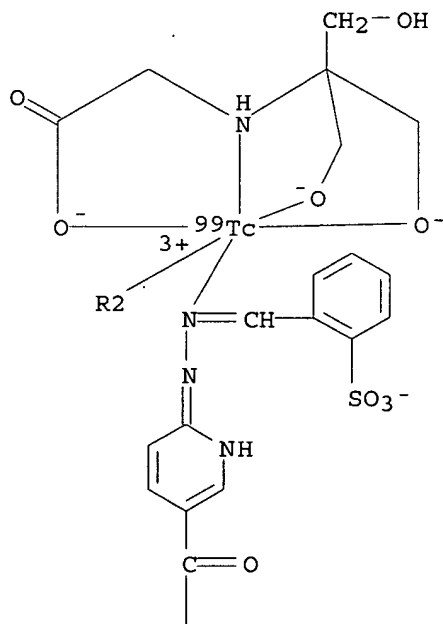
● 2 H⁺

● 3 Na⁺

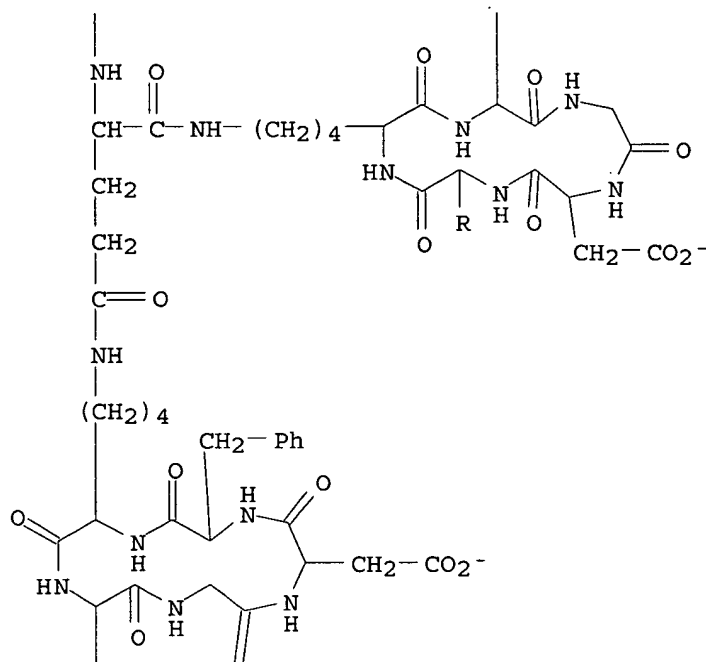
RN 250614-24-5 HCAPLUS

CN Technetate (6-) -99Tc, [N-[2-hydroxy-1,1-bis[(hydroxy-κO)methyl]ethyl]glycinato(3-)-κN,κO] [[3,3',3''-(phosphinidyne-κP)tris[benzenesulfonato]](3-)] [[5,5'-(N-[[6-[[[(2-sulfophenyl)methylene]hydrazino-κN2]-3-pyridinyl]carbonyl]-L-glutamoyl]bis[cyclo(L-arginylglycyl-L-α-aspartyl-D-phenylalanyl-L-lysylato)]](3-))-, trisodium trihydrogen (9CI) (CA INDEX NAME)

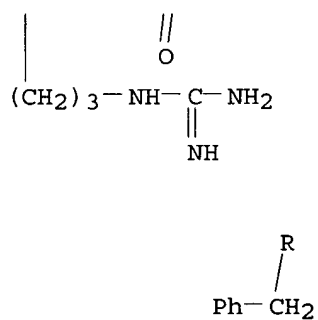
PAGE 1-A



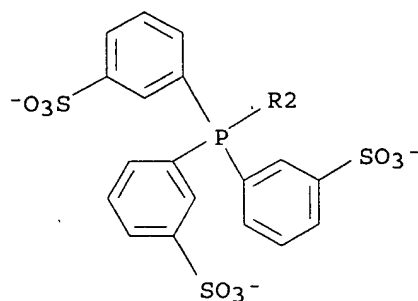
PAGE 2-A



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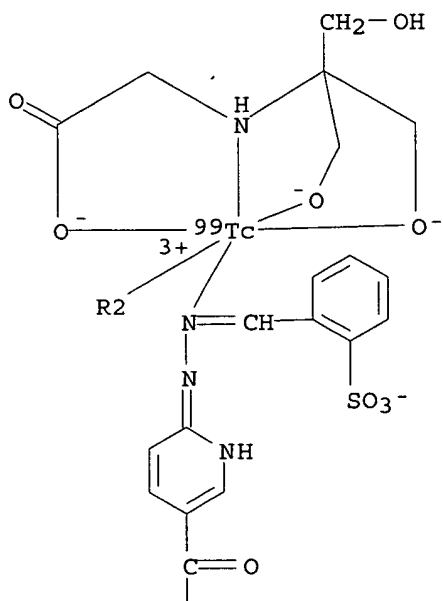
PAGE 4-A

● 3 H⁺● 3 Na⁺

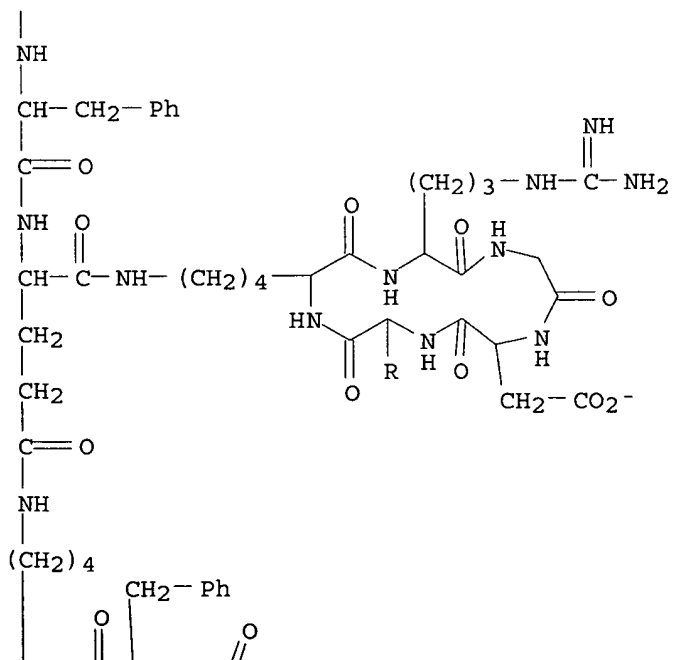
RN 250614-25-6 HCAPLUS

CN Technetate (6-) -99Tc, [N-[2-hydroxy-1,1-bis[(hydroxy-
 κO)methyl]ethyl]glycinato(3-)-κN,κO] [[3,3',3''-
 (phosphinidyne-κP)tris[benzenesulfonato]](3-)] [[5,5'-[N-[[6-[[2-
 sulfophenyl)methylene]hydrazino-κN2]-3-pyridinyl]carbonyl]-L-
 phenylalanyl-L-glutamoyl]bis[cyclo(L-arginylglycyl-L-α-aspartyl-D-
 phenylalanyl-L-lysylato)]](3-)]-, trisodium trihydrogen (9CI) (CA INDEX
 NAME)

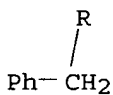
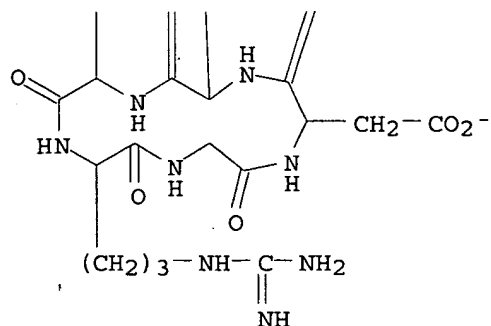
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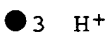
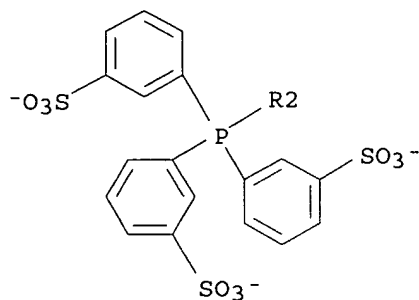
PAGE 2-A



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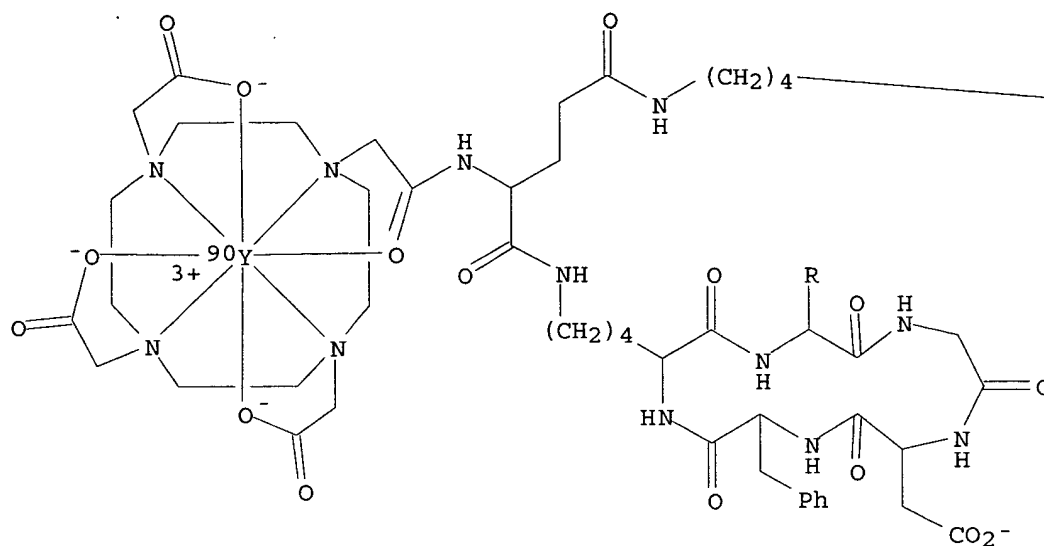


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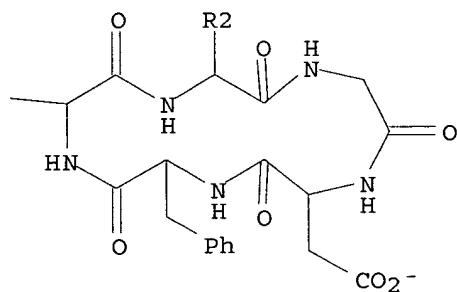


RN 250614-38-1 HCAPLUS
 CN Yttrate(2-)-90Y, [[5,5'-[N-[[4,7,10-tris[(carboxy-κO)methyl]-1,4,7,10-tetraazacyclododec-1-yl-κN1,κN4,κN7,κN10]acetyl-κO]-L-glutamoyl]bis[cyclo(L-arginylglycyl-L-α-aspartyl-D-phenylalanyl-L-lysylato)]](5-)]-, dihydrogen (9CI) (CA INDEX NAME)

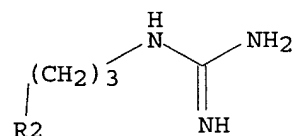
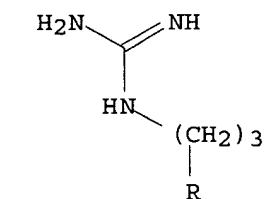
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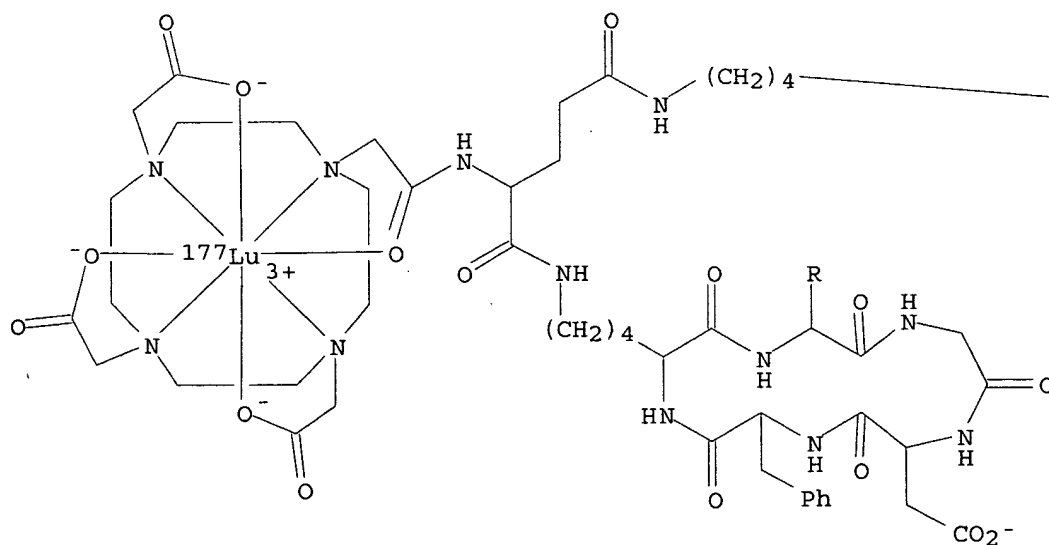
PAGE 2-A



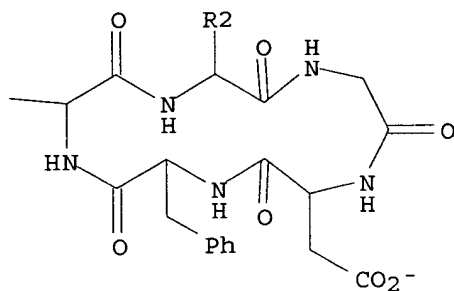
● 2 H^+

RN 250614-39-2 HCAPLUS
 CN Lutetate(2-)- ^{177}Lu , [[5,5'-[N-[[4,7,10-tris[(carboxy- κO)methyl]-1,4,7,10-tetraazacyclododec-1-yl- $\kappa\text{N}1$, $\kappa\text{N}4$, $\kappa\text{N}7$, $\kappa\text{N}10$]acetyl- κO]-L-glutamoyl]bis[cyclo(L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-L-lysylato)]](5-)]-, dihydrogen (9CI) (CA INDEX NAME)

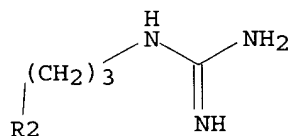
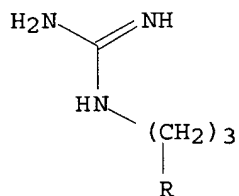
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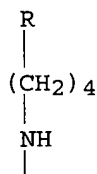
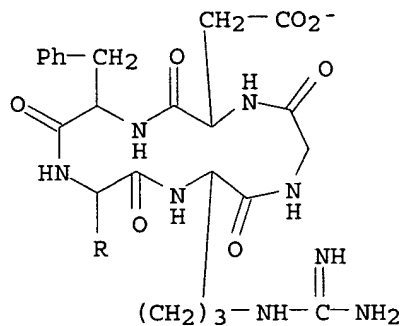


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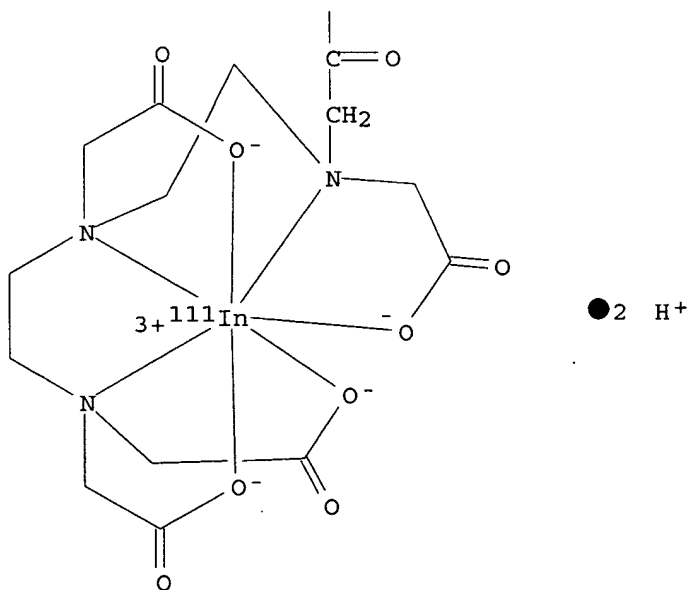
● 2 H⁺

RN 250614-41-6 HCAPLUS
 CN Indate(2-)-111In, [cyclo[L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-N6-[N-[2-[2-[bis[(carboxy- κ O)methyl]amino- κ N]ethyl][(carboxy- κ O)methyl]amino- κ N]ethyl]-N-[(carboxy- κ O)methyl]glycyl- κ N, κ O]-L-lysylato(5-)]], dihydrogen (9CI) (CA INDEX NAME)

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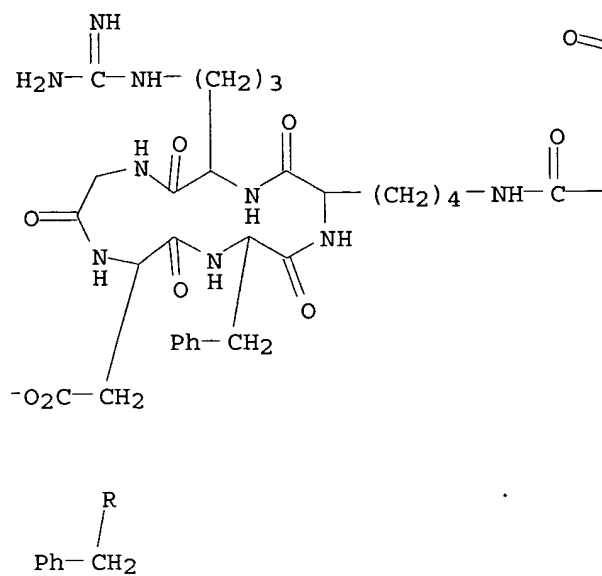


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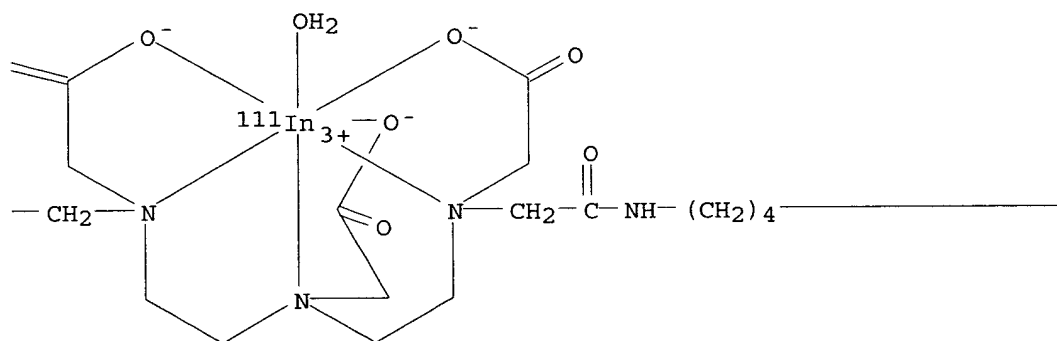


RN 250614-42-7 HCAPLUS
 CN Indate(2-)-111In, aqua[[1',1'''-[[[(carboxy-κO)methyl]imino-κN]di-2,1-ethanediyl]bis[cyclo[L-arginylglycyl-L-α-aspartyl-D-phenylalanyl-N6-[N-[(carboxy-κO)methyl]glycyl-κN]-L-lysylato]]](5-)]-, dihydrogen (9CI) (CA INDEX NAME)

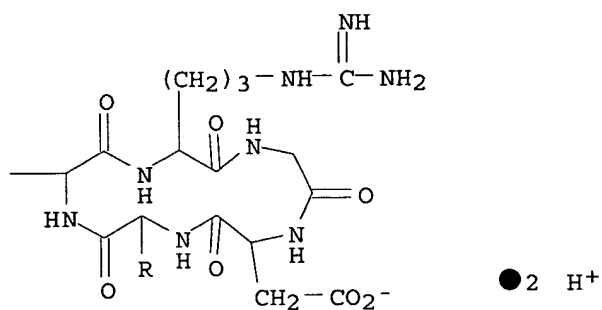
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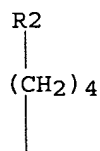
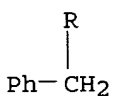
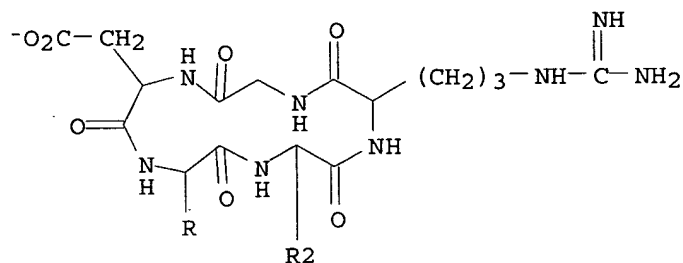


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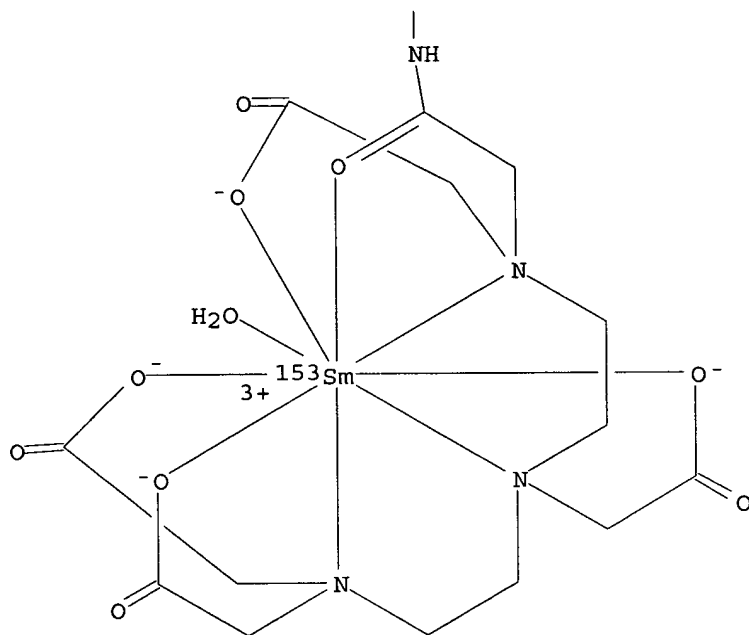


RN 250614-43-8 HCAPLUS
 CN Samarate(2-)-153Sm, aqua[cyclo[L-arginylglycyl-L-α-aspartyl-D-phenylalanyl-N6-[N-[2-[[2-[bis[(carboxy-κO)methyl]amino-κN]ethyl][(carboxy-κO)methyl]amino-κN]ethyl]-N-[(carboxy-κO)methyl]glycyl-κN,κO]-L-lysylato(5-)]], dihydrogen (9CI) (CA INDEX NAME)

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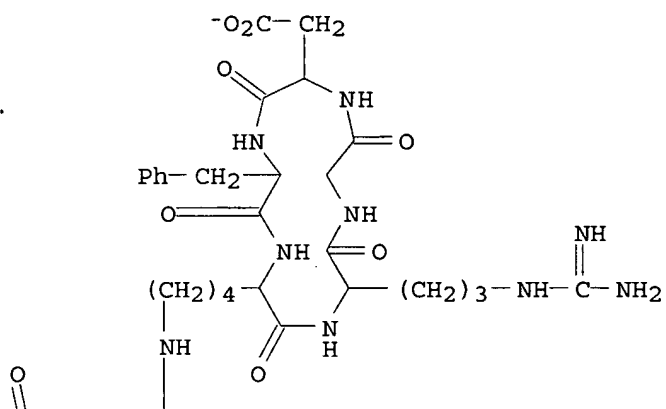


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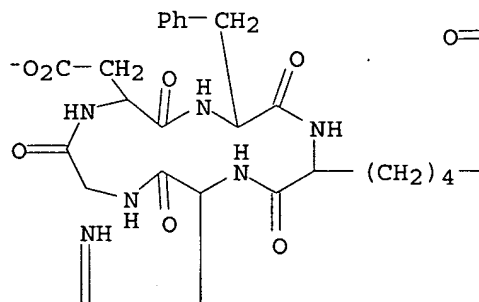
● 2 H⁺

RN 250614-44-9 HCAPLUS
 CN Samarate(2-)-153Sm, [[1',1'''-[[[(carboxy-κO)methyl]imino-κN]di-2,1-ethanediyl]bis[cyclo[L-arginylglycyl-L-α-aspartyl-D-phenylalanyl-N6-[N-[(carboxy-κO)methyl]glycyl-κN]-L-lysylato]]](5-)]-, dihydrogen (9CI) (CA INDEX NAME)

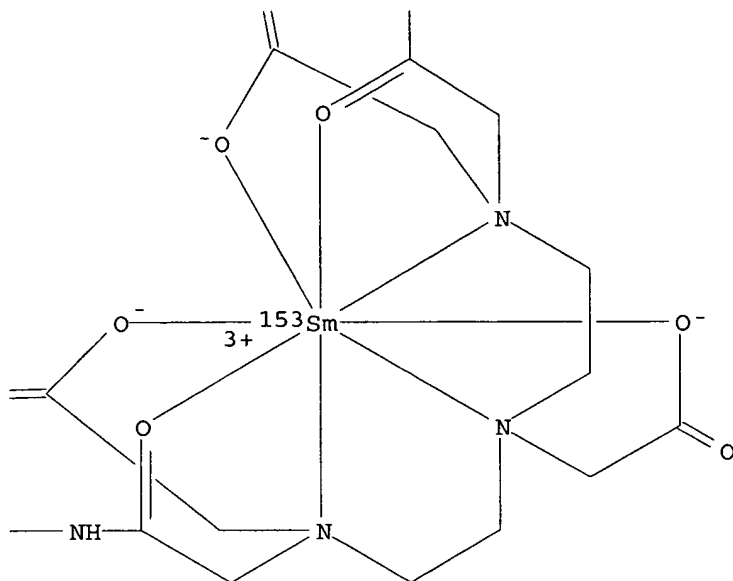
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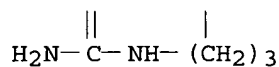
PAGE 2-A



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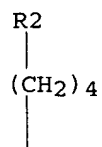
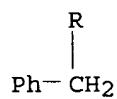
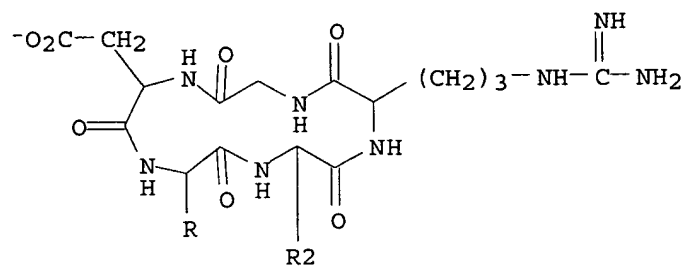


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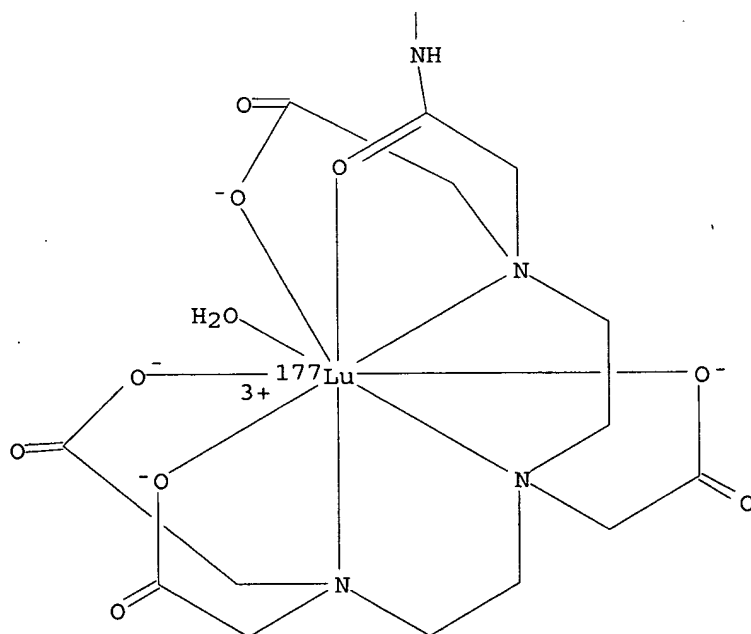
● 2 H⁺

RN 250614-46-1 HCAPLUS
 CN Lutetate(2-)-177Lu, aqua[cyclo[L-arginylglycyl-L-α-aspartyl-D-phenylalanyl-N6-[N-[2-[2-[bis[(carboxy-κO)methyl]amino-κN]ethyl][(carboxy-κO)methyl]amino-κN]ethyl]-N-[(carboxy-κO)methyl]glycyl-κN,κO]-L-lysylato(5-)]]-, dihydrogen (9CI) (CA INDEX NAME)

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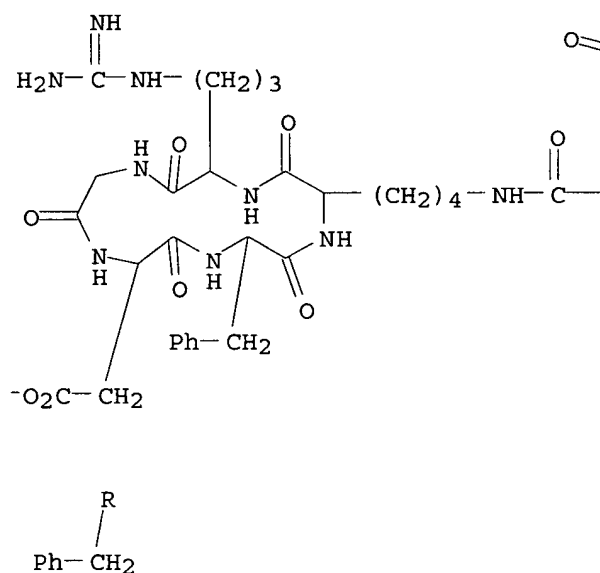


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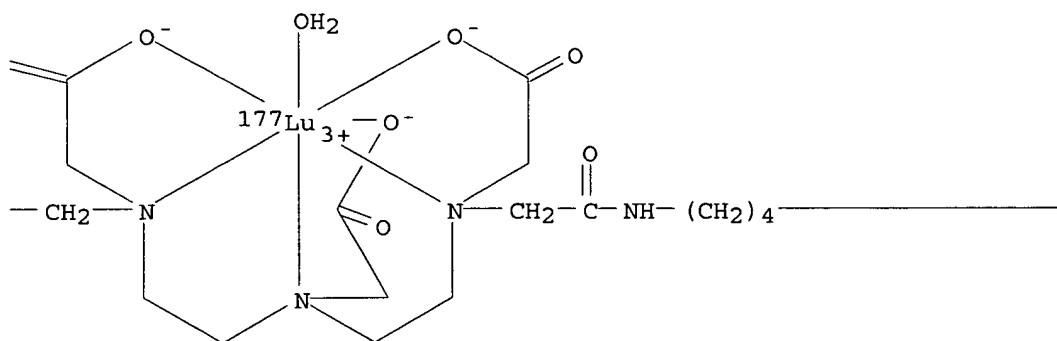
● 2 H⁺

RN 250614-47-2 HCAPLUS
 CN Lutetate(2-)-177Lu, aqua[[1',1'''-[[[(carboxy-κO)methyl]imino-κN]di-2,1-ethanediyl]bis[cyclo[L-arginylglycyl-L-α-aspartyl-D-phenylalanyl-N6-[N-[(carboxy-κO)methyl]glycyl-κN]-L-lysylato]]](5-)]-, dihydrogen (9CI) (CA INDEX NAME)

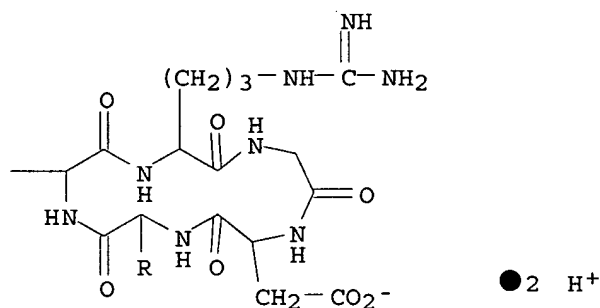
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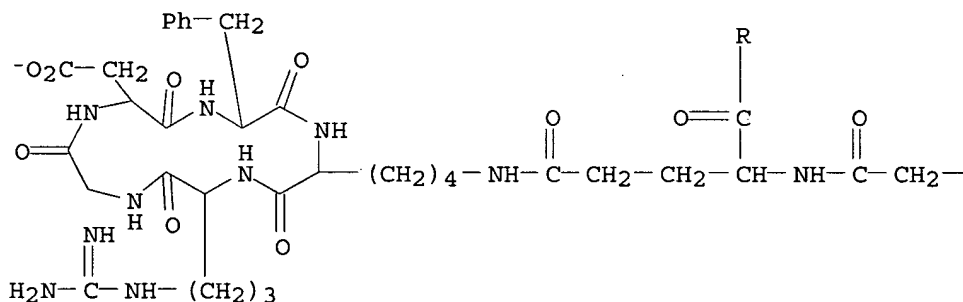


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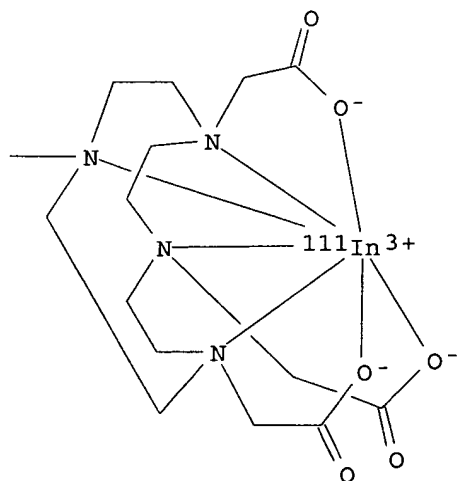


RN 851024-71-0 HCAPLUS
 CN Indate(2-)-111In, [[5,5'-[N-[[4,7,10-tris[(carboxy-κO)methyl]-1,4,7,10-tetraazacyclododec-1-yl-κN1,κN4,κN7,κN10]acetyl]-L-glutamoyl]bis[cyclo[L-arginylglycyl-L-α-aspartyl-D-phenylalanyl-L-lysylato]]](5-)]-, dihydrogen (9CI) (CA INDEX NAME)

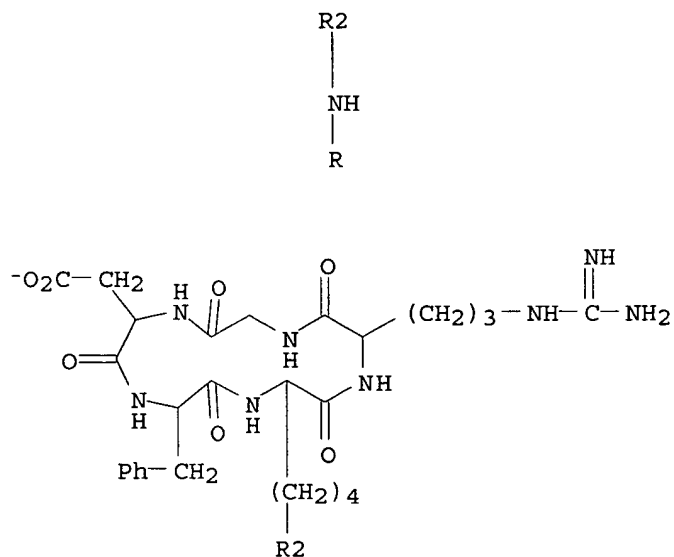
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● 2 H⁺

IT 161552-03-0

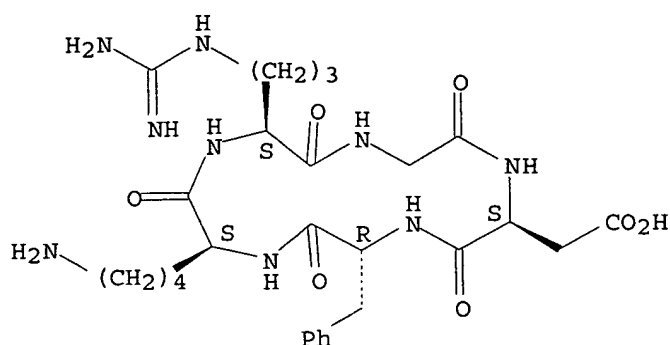
RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of peptide derivs. for the imaging of angiogenic disorders and the treatment of cancer in combination therapy)

RN 161552-03-0 HCAPLUS

CN Cyclo(L-arginylglycyl-L-α-aspartyl-D-phenylalanyl-L-lysyl) (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



IT 250612-41-0P 250612-42-1P 250612-43-2P
250612-44-3P 250612-46-5P 250612-48-7P
250612-50-1P 250612-82-9P

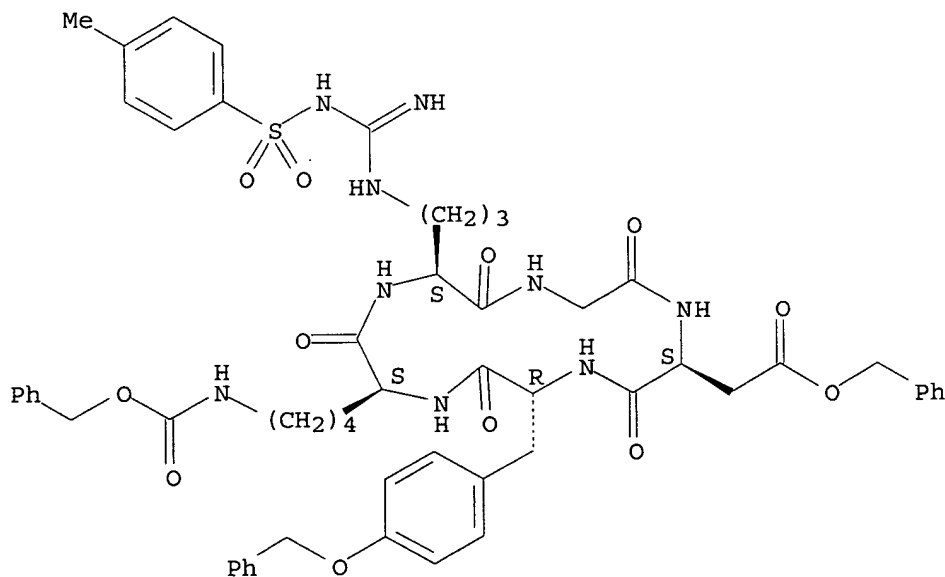
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of peptide derivs. for the imaging of angiogenic disorders and the treatment of cancer in combination therapy)

RN 250612-41-0 HCAPLUS

CN Cyclo[L- α -aspartyl-O-(phenylmethyl)-D-tyrosyl-N6-[(phenylmethoxy)carbonyl]-L-lysyl-N5-[imino[[4-methylphenyl)sulfonyl]amino]methyl]-L-ornithylglycyl], phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 250612-42-1 HCAPLUS

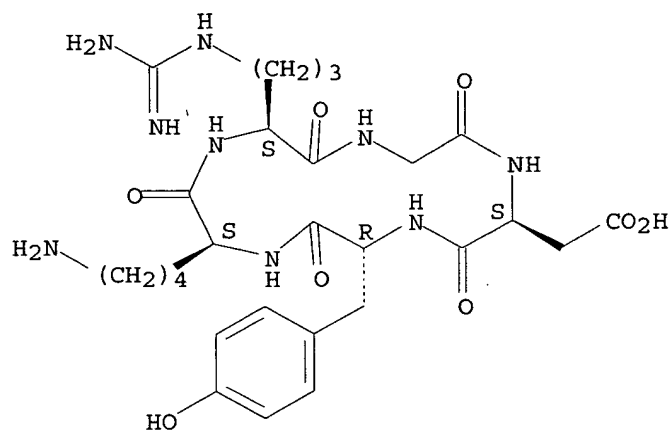
CN Cyclo(L-arginylglycyl-L- α -aspartyl-D-tyrosyl-L-lysyl), bis(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 217099-14-4

CMF C27 H41 N9 O8

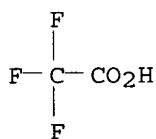
Absolute stereochemistry.



CM 2

CRN 76-05-1

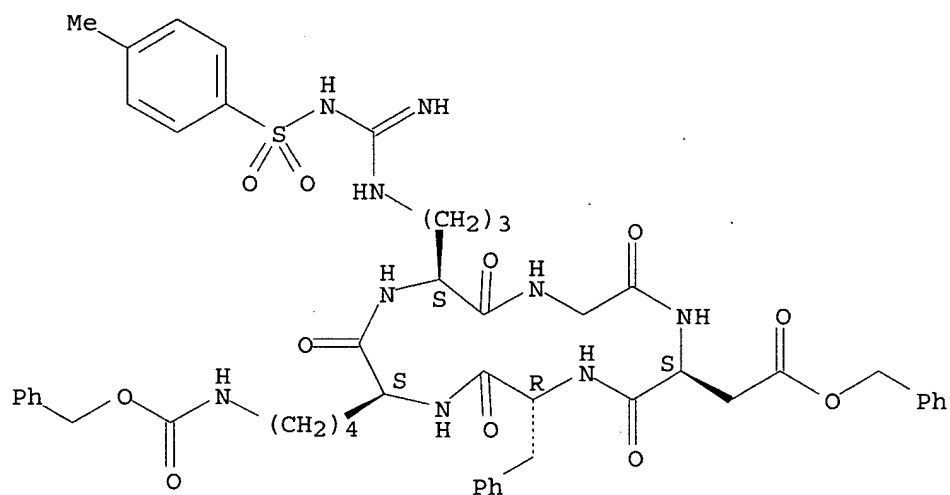
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RN 250612-43-2 HCAPLUS

CN Cyclo[L-α-aspartyl-D-phenylalanyl-N6-[(phenylmethoxy) carbonyl]-L-lysyl-N5-[imino[[4-methylphenyl)sulfonyl]amino]methyl]-L-ornithylglycyl], phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 250612-44-3 HCAPLUS

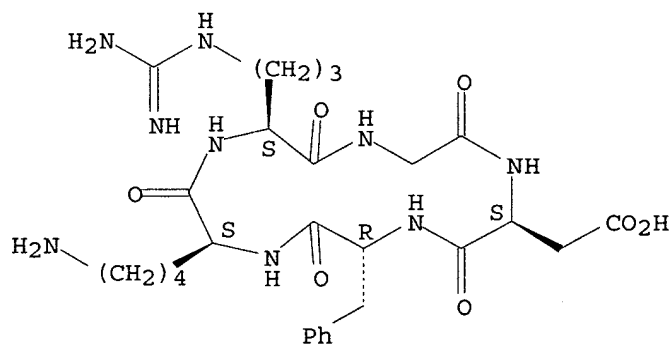
CN Cyclo(L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-L-lysyl),
bis(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 161552-03-0

CMF C27 H41 N9 O7

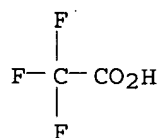
Absolute stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2

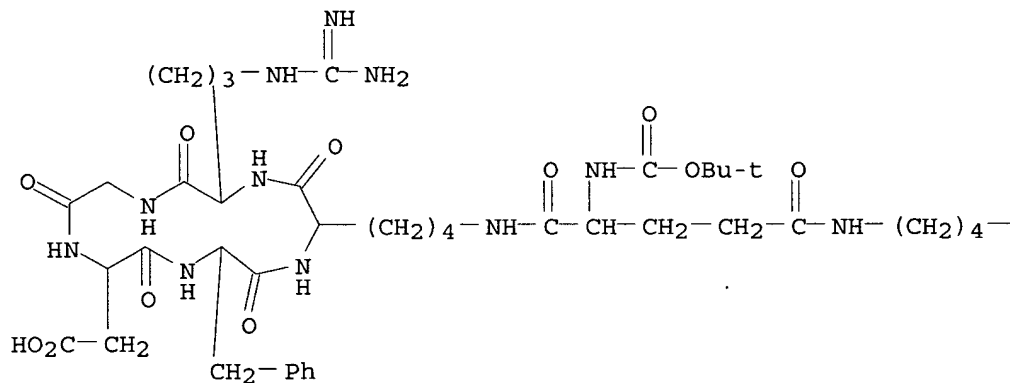


RN 250612-46-5 HCAPLUS
 CN Cyclo(L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-L-lysyl),
 5,5'-[N-[(1,1-dimethylethoxy)carbonyl]-L-glutamoyl]bis-,
 bis(trifluoroacetate) (9CI) (CA INDEX NAME)

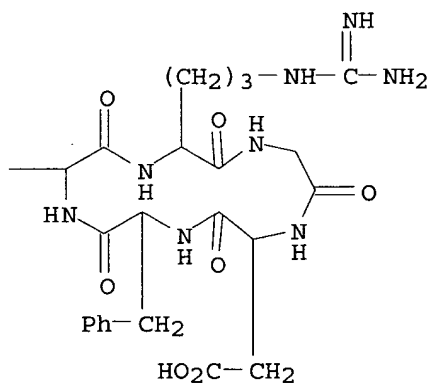
CM 1

CRN 250612-45-4
 CMF C64 H95 N19 O18

PAGE 1-A

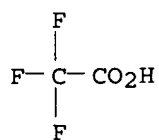


PAGE 1-B



CM 2

CRN 76-05-1
 CMF C2 H F3 O2

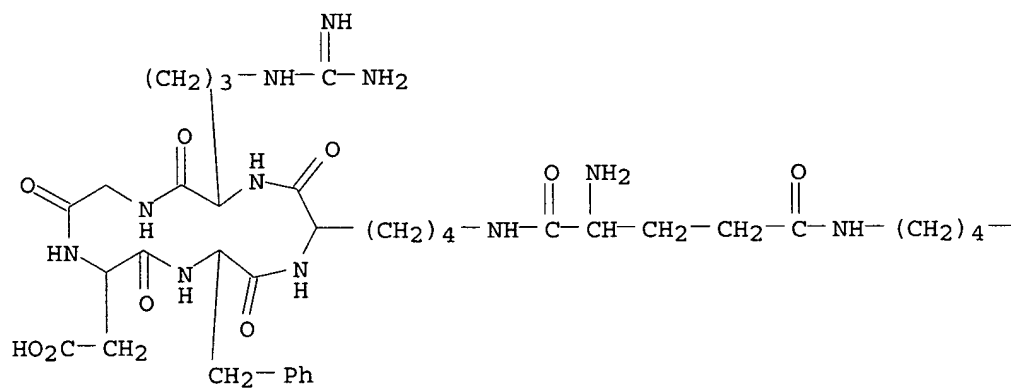


RN 250612-48-7 HCAPLUS
 CN Cyclo(L-arginylglycyl-L-α-aspartyl-D-phenylalanyl-L-lysyl),
 5,5'-L-glutamoylbis-, tris(trifluoroacetate) (9CI) (CA INDEX NAME)

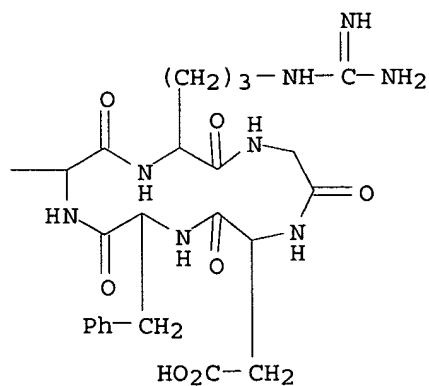
CM 1

CRN 250612-47-6
 CMF C59 H87 N19 O16

PAGE 1-A

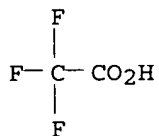


PAGE 1-B



CM 2

CRN 76-05-1
CMF C2 H F3 O2

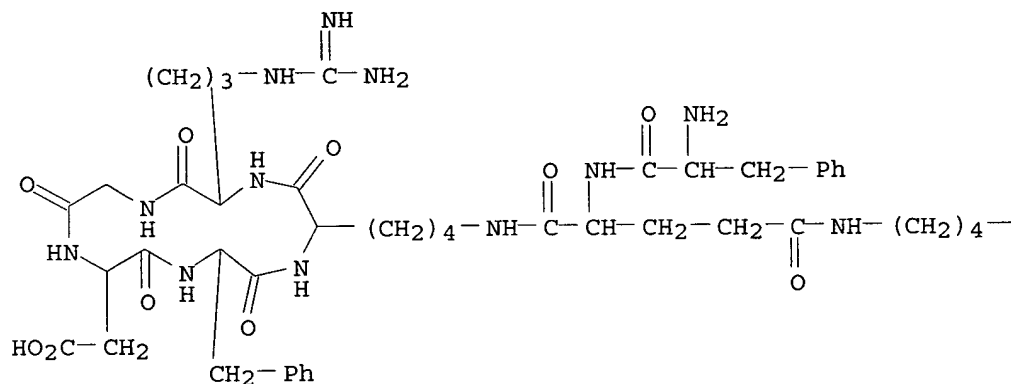


RN 250612-50-1 HCAPLUS
CN Cyclo(L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-L-lysyl),
5,5'-(L-phenylalanyl-L-glutamoyl)bis-, tris(trifluoroacetate) (9CI) (CA
INDEX NAME)

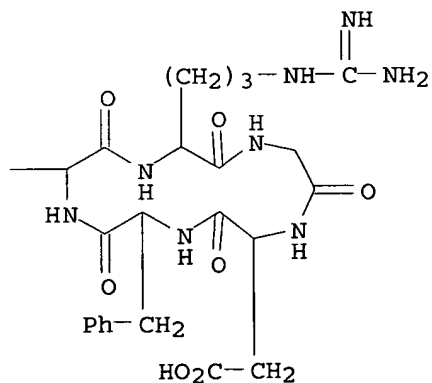
CM 1

CRN 250612-49-8
CMF C68 H96 N20 O17

PAGE 1-A



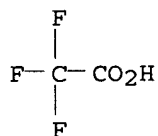
PAGE 1-B



CM 2

CRN 76-05-1

CMF C2 H F3 O2



RN 250612-82-9 HCAPLUS

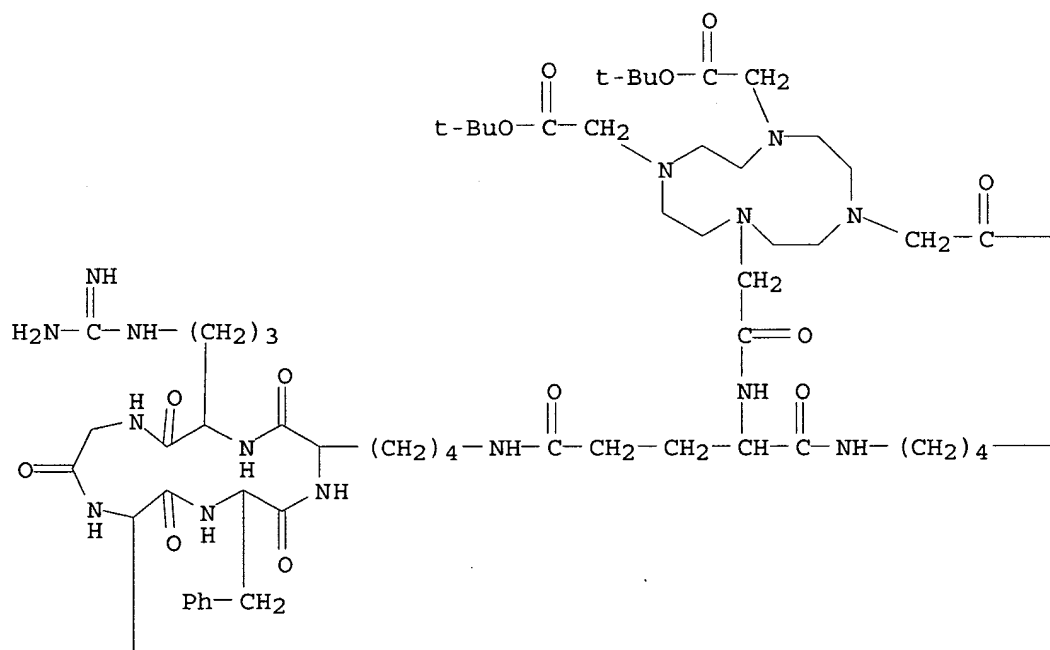
CN Cyclo(L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-L-lysyl),
 5,5'-[N-[[4,7,10-tris[2-(1,1-dimethylethoxy)-2-oxoethyl]-1,4,7,10-
 tetraazacyclododec-1-yl]acetyl]-L-glutamoyl]bis-, bis(trifluoroacetate)
 (9CI) (CA INDEX NAME)

CM 1

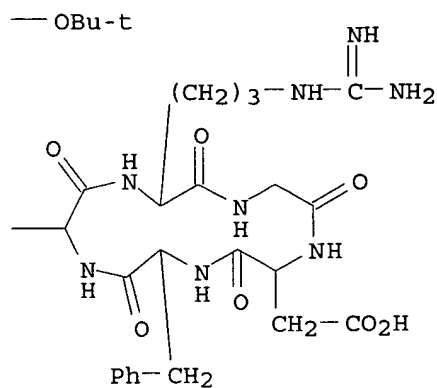
CRN 250612-81-8

CMF C87 H137 N23 O23

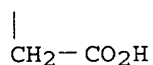
PAGE 1-A



PAGE 1-B

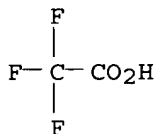


PAGE 2-A



CM 2

CRN 76-05-1
CMF C2 H F3 O2



REFERENCE COUNT: 110 THERE ARE 110 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 32 OF 43 HCAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2003:174212 HCAPLUS
 DOCUMENT NUMBER: 138:210356
 TITLE: Gas microsphere liposome composites for ultrasound imaging and ultrasound stimulated drug release
 INVENTOR(S): Carpenter, Alan P.; Slack, Gregory C.
 PATENT ASSIGNEE(S): USA
 SOURCE: U.S. Pat. Appl. Publ., 19 pp.
 CODEN: USXXCO

DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003044354	A1	20030306	US 2001-931317	20010816
PRIORITY APPLN. INFO.:			US 2001-931317	20010816

AB Formulations comprising a gas microsphere liposome composite suspended in a medium, wherein the gas microsphere liposome composite comprises: a gas-filled microsphere; at 1 of a lipid and a surfactant adsorbed onto the surface of the gas-filled microsphere; and liquid-filled liposomes attached to the lipid or surfactant are described. Methods of preparing the same and using them in ultrasound imaging are also described. The present invention also comprises use of the same in treating heart disease, inflammation, infection, cancer or thromboembolic disease in a patient. A saline glycerol solution (100 mL) was prepared including glycerol (10 mL) and NaCl (680 mg) in water (to a final volume of 100 mL). Dipalmitoylphosphatidylcholine (40.0 mg), MPEG500-dipalmitoyl phosphatidylethanolamine (30.0 mg), and DPPA (4.5 mg) were mixed with propylene glycol (10 mL) and placed in a hot water bath (70°) and sonicated for 15 min until the solution cleared. The saline/glycerol solution was then added to bring the mixture to final volume of 100 mL, and the suspension was mixed well. The suspension (1.6 mL) was transferred into a 2 mL borosilicate glass vial. The headspace was purged with perfluoropropane gas, and the vial was stoppered and sealed. The vial containing the lipid suspension was shaken for 45 s by using the Ionoos Ionomix. After shaking, the suspension became milky white.

IC ICM A61B008-00
 INCL 424009510
 CC 63-6 (Pharmaceuticals)
 Section cross-reference(s): 8, 9

IT **Integrins**
 RL: BSU (Biological study, unclassified); BIOL (Biological study) (α IIB β 3; gas microsphere liposome composites for ultrasound imaging and ultrasound stimulated drug release)

IT **Integrins**
 RL: BSU (Biological study, unclassified); BIOL (Biological study) (α V β 3; gas microsphere liposome composites for ultrasound imaging and ultrasound stimulated drug release)

IT **Integrins**
 RL: BSU (Biological study, unclassified); BIOL (Biological study) (α V β 5; gas microsphere liposome composites for ultrasound imaging and ultrasound stimulated drug release)

IT **250612-24-9P 250612-25-0P 500577-49-1P 500577-50-4P 500577-52-6P 500577-57-1P**
 RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (gas microsphere liposome composites for ultrasound imaging and ultrasound stimulated drug release)

IT 50-18-0, Cyclophosphamide 57-10-3, Hexadecanoic acid, biological studies 59-05-2, Methotrexate 63-89-8, Dipalmitoylphosphatidylcholine 143-02-2, Palmitoyl sulfate 143-07-7, Dodecanoic acid, biological studies 151-41-7 4235-95-4 7091-44-3 9000-69-5, Pectin 9002-89-5, Polyvinyl alcohol 9003-39-8, Polyvinylpyrrolidone 9004-34-6, Cellulose, biological studies 9004-54-0, Dextran, biological studies 10549-76-5D, Tetrabutylammonium, salts 11138-66-2, Xanthan gum 15663-27-1, Cisplatin 15853-37-9D, Tetrabutylphosphonium, salts 18194-24-6, Dimyristoylphosphatidylcholine 18194-25-7,

Dilauroylphosphatidylcholine 18198-39-5D, Tetraphenylphosphonium, salts 19524-73-3D, Tetraoctylammonium, salts 19698-29-4, DPPA 20256-54-6D, Tetrahexylammonium, salts 23214-92-8, Doxorubicin 25316-40-9, Adriamycin 25322-68-3, Polyethylene glycol 25322-69-4, Polypropylene glycol 45286-86-0D, Tetrahexylphosphonium, salts 45308-00-7D, Tetraoctylphosphonium, salts 48078-03-1D, Tetradecylammonium, salts 95058-81-4, Gemcitabine 125317-39-7, Navelbine 139639-23-9, Tissue plasminogen activator 170902-47-3, Roxifiban 182280-70-2 185243-69-0, Enbrel 188627-80-7, Integrelin 205494-72-0

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gas microsphere liposome composites for ultrasound imaging and ultrasound stimulated drug release)

IT 75472-90-1 159156-96-4 **161552-03-0 500577-51-5**
500577-55-9 500577-56-0

RL: RCT (Reactant); RACT (Reactant or reagent)
(in phospholipid-cyclic peptide preparation; gas microsphere liposome composites for ultrasound imaging and ultrasound stimulated drug release)

IT **499995-17-4P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(in phospholipid-cyclic peptide preparation; gas microsphere liposome composites for ultrasound imaging and ultrasound stimulated drug release)

IT **250612-24-9P 250612-25-0P**

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(gas microsphere liposome composites for ultrasound imaging and ultrasound stimulated drug release)

IT **161552-03-0 500577-51-5**

RL: RCT (Reactant); RACT (Reactant or reagent)
(in phospholipid-cyclic peptide preparation; gas microsphere liposome composites for ultrasound imaging and ultrasound stimulated drug release)

IT **499995-17-4P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(in phospholipid-cyclic peptide preparation; gas microsphere liposome composites for ultrasound imaging and ultrasound stimulated drug release)

IT **250612-24-9P 250612-25-0P**

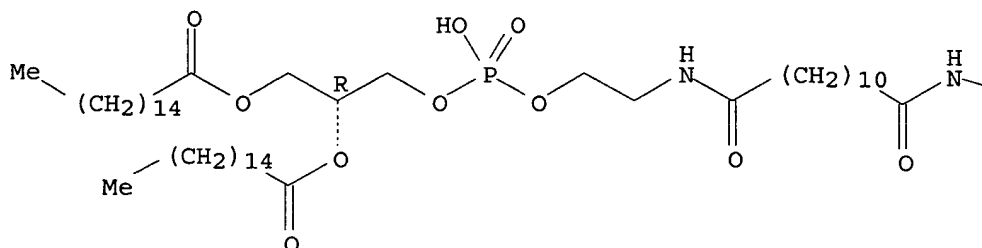
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(gas microsphere liposome composites for ultrasound imaging and ultrasound stimulated drug release)

RN 250612-24-9 HCAPLUS

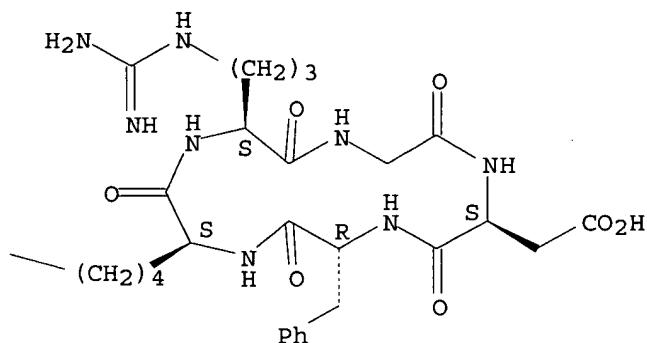
CN Cyclo[L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-N6-[(20R)-17-hydroxy-17-oxido-1,12,23-trioxo-20-[(1-oxohexadecyl)oxy]-16,18,22-trioxa-13-aza-17-phosphaoctatriacont-1-yl]-L-lysyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



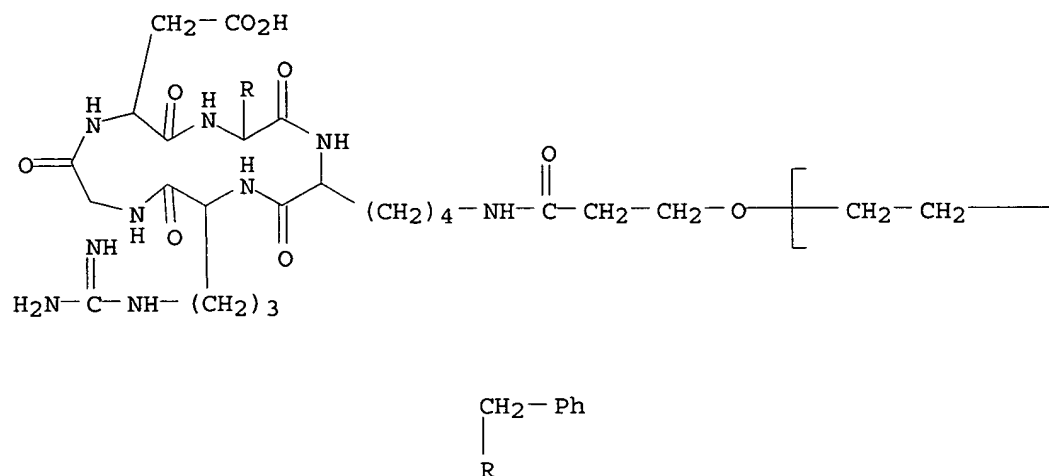
PAGE 1-B



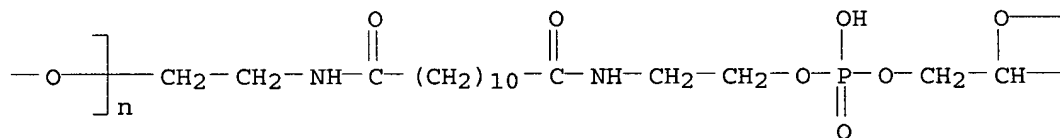
RN 250612-25-0 HCAPLUS

CN Cyclo[L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-N6-(3-hydroxy-1-oxopropyl)-L-lysyl], ether with α -[(23R)-20-hydroxy-20-oxido-4,15,26-trioxo-23-[(1-oxohexadecyl)oxy]-19,21,25-trioxa-3,16-diaza-20-phosphahentriacont-1-yl]- ω -hydroxypoly(oxy-1,2-ethanediyl) (9CI)
(CA INDEX NAME)

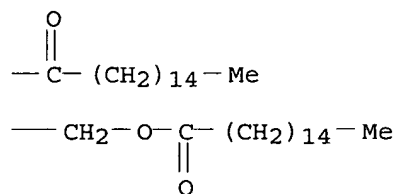
PAGE 1-A



PAGE 1-B



PAGE 1-C



IT 161552-03-0 500577-51-5

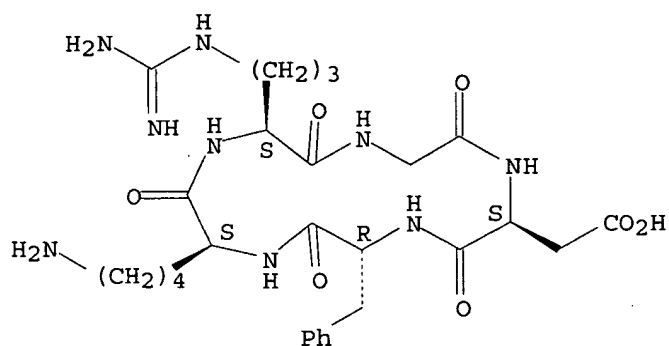
RL: RCT (Reactant); RACT (Reactant or reagent)

(in phospholipid-cyclic peptide preparation; gas microsphere liposome composites for ultrasound imaging and ultrasound stimulated drug release)

RN 161552-03-0 HCAPLUS

CN Cyclo(L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-L-lysyl) (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



RN 500577-51-5 HCAPLUS

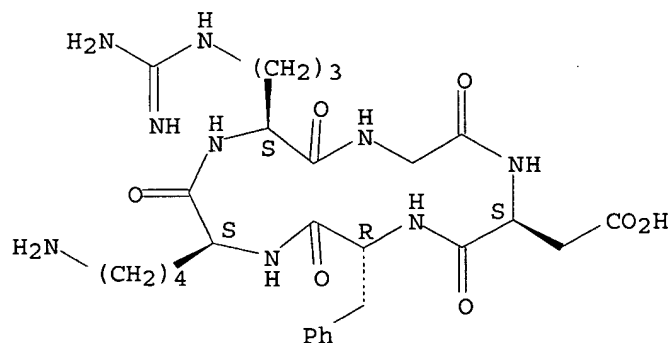
CN Cyclo(L-arginylglycyl-L-α-aspartyl-D-phenylalanyl-L-lysyl),
mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 161552-03-0

CMF C27 H41 N9 O7

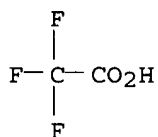
Absolute stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2

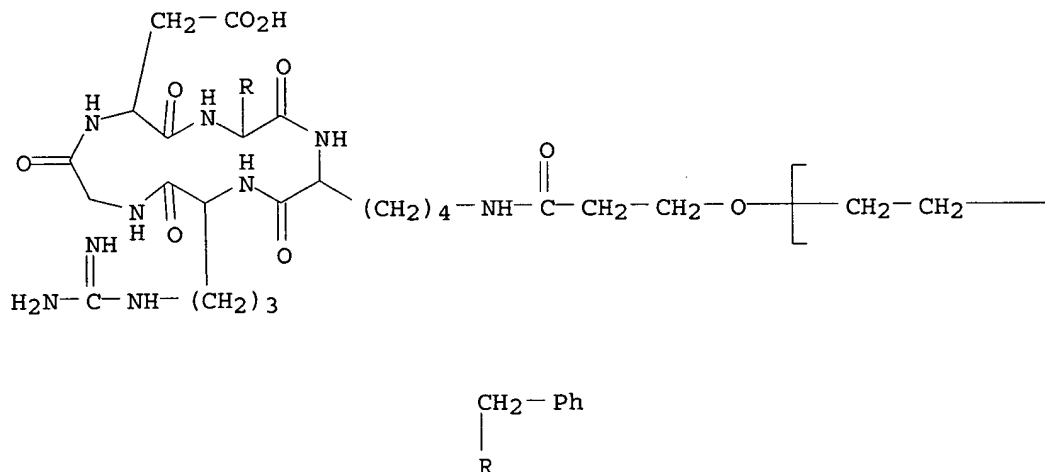


IT 499995-17-4P

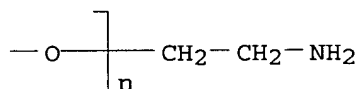
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)

(in phospholipid-cyclic peptide preparation; gas microsphere liposome
composites for ultrasound imaging and ultrasound stimulated drug

PAGE 1-A



PAGE 1-B



L47 ANSWER 33 OF 43 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:154287 HCAPLUS
DOCUMENT NUMBER: 138:210306
TITLE: Gas microsphere-liposome composites
INVENTOR(S): Carpenter, Alan P., Jr.; Slack, Gregory C.
PATENT ASSIGNEE(S): Bristol-Myers Squibb Pharma Company, USA
SOURCE: PCT Int. Appl., 53 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2003015831	A1	20030227	WO 2001-US25685	20010816
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,				

CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
 GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
 LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,
 RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ,
 VN, YU, ZA, ZW
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
 DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
 BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
 CA 2456988 AA 20030227 CA 2001-2456988 20010816
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 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
 BR 2001017106 A 20040817 BR 2001-17106 20010816
 JP 2005505532 T2 20050224 JP 2003-520788 20010816
 CN 1620314 A 20050525 CN 2001-823708 20010816
 NO 2004000654 A 20040514 NO 2004-654 20040213
 PRIORITY APPLN. INFO.: WO 2001-US25685 W 20010816
 AB A formulation that includes a gas microsphere-liposome composite (MSLC)
 suspended in a medium is provided. A gas microsphere-liposome composite
 comprises a gas-filled microsphere, at least one of a lipid and a
 surfactant adsorbed onto the surface of the gas-filled microsphere, and
 liquid-filled liposomes attached to the lipid or surfactant. The
 formulations are useful for ultrasound imaging and for treating heart
 disease, inflammation, infection, cancer or thromboembolic disease in a
 patient. For example, **doxorubicin** (100-200 mg/mL) was added to
 a perfluoropropane-containing phospholipid contrast agent composition
 (preparation
 given) to obtain a MSLC suspension for therapeutic uses.
 IC ICM A61K049-22
 ICS A61K041-00
 CC 63-6 (Pharmaceuticals)
 Section cross-reference(s): 1, 8
 IT **Integrins**
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (α IIb β 3, ligands for binding to; preparation of gas
 microsphere-liposome composites for delivery of diagnostic and
 therapeutic agents)
 IT **Integrins**
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (α v β 3, ligands for binding to; preparation of gas
 microsphere-liposome composites for delivery of diagnostic and
 therapeutic agents)
 IT **Integrins**
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (α v β 5, ligands for binding to; preparation of gas
 microsphere-liposome composites for delivery of diagnostic and
 therapeutic agents)
 IT 5681-36-7, Dipalmitoylphosphatidylethanolamine 159156-96-4 216222-86-5
 250612-44-3 355150-15-1 355150-19-5 415927-76-3
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (preparation of gas microsphere-liposome composites for delivery of
 diagnostic and therapeutic agents)
 IT **499995-17-4P**
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)
 (preparation of gas microsphere-liposome composites for delivery of
 diagnostic and therapeutic agents)
 IT 50-18-0, Cyclophosphamide 59-05-2, Methotrexate 63-89-8,
 Dipalmitoylphosphatidylcholine 76-19-7, Perfluoropropane 112-53-8D,
 Dodecanol, esters with carboxylic acids 143-02-2, Palmityl sulfate

151-41-7 355-25-9, Perfluorobutane 2644-64-6,
 Dipalmitoylphosphatidylcholine 4235-95-4 9000-69-5, Pectin
 9002-89-5, Polyvinyl alcohol 9003-39-8, Polyvinyl pyrrolidone
 9004-34-6, Cellulose, biological studies 9004-53-9, Dextrin
 10549-76-5, Tetrabutylammonium 11138-66-2, Xanthan gum 15663-27-1,
 Cisplatin 15853-37-9, Tetrabutylphosphonium 18194-25-7,
 Dilauroylphosphatidylcholine 18198-39-5, Tetraphenylphosphonium
 18656-38-7, Dimyristoylphosphatidylcholine 19524-73-3,
 Tetraoctylammonium 19698-29-4, Dipalmitoylphosphatidic acid
 20256-54-6, Tetrahexylammonium 23214-92-8, **Doxorubicin**
 25316-40-9, Adriamycin 25322-68-3, Polyethylene glycol 25322-69-4,
 Polypropylene glycol 36653-82-4D, Palmityl alcohol, esters with
 carboxylic acids 45286-86-0, Tetrahexylphosphonium 45308-00-7,
 Tetraoctylphosphonium 48078-03-1, Tetradecylammonium 95058-81-4,
 Gemcitabine 125317-39-7, Navelbine 139639-23-9, Tissue plasminogen
 activator 170902-47-3, Roxifiban 185243-69-0, Enbrel 188627-80-7,
 Integrelin 459429-07-3

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(preparation of gas microsphere-liposome composites for delivery of
 diagnostic and therapeutic agents)

IT 250612-24-9P 250612-25-0P 499995-15-2P 499995-16-3P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
 study); PREP (Preparation); USES (Uses)

(targeting moiety; preparation of gas microsphere-liposome composites for
 delivery of diagnostic and therapeutic agents)

IT 250612-44-3

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of gas microsphere-liposome composites for delivery of
 diagnostic and therapeutic agents)

IT 499995-17-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)

(preparation of gas microsphere-liposome composites for delivery of
 diagnostic and therapeutic agents)

IT 250612-24-9P 250612-25-0P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
 study); PREP (Preparation); USES (Uses)

(targeting moiety; preparation of gas microsphere-liposome composites for
 delivery of diagnostic and therapeutic agents)

IT 250612-44-3

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of gas microsphere-liposome composites for delivery of
 diagnostic and therapeutic agents)

RN 250612-44-3 HCAPLUS

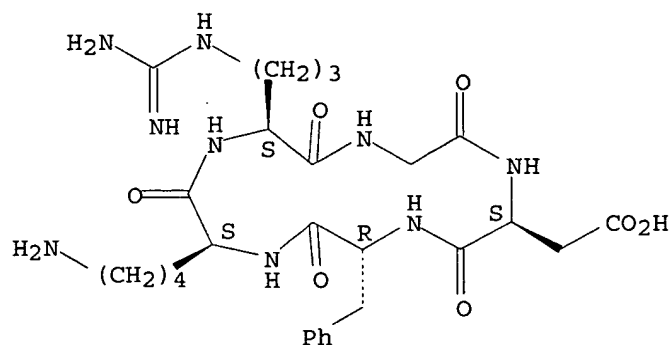
CN Cyclo(L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-L-lysyl),
 bis(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 161552-03-0

CMF C27 H41 N9 O7

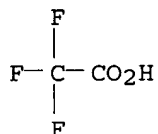
Absolute stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2



IT 499995-17-4P

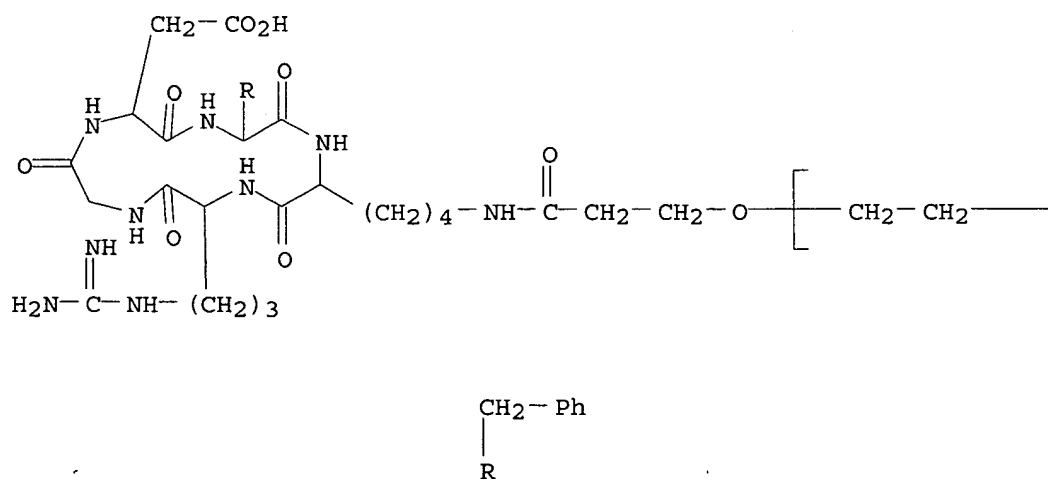
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of gas microsphere-liposome composites for delivery of diagnostic and therapeutic agents)

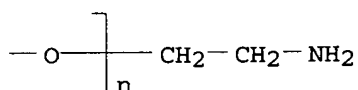
RN 499995-17-4 HCAPLUS

CN Poly(oxy-1,2-ethanediyl), α -(2-aminoethyl)- ω -hydroxy-, ether with cyclo[L-arginylglycyl-1- α -aspartyl-D-phenylalanyl-N6-(3-hydroxy-1-oxopropyl)-L-lysyl] (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



IT 250612-24-9P 250612-25-0P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

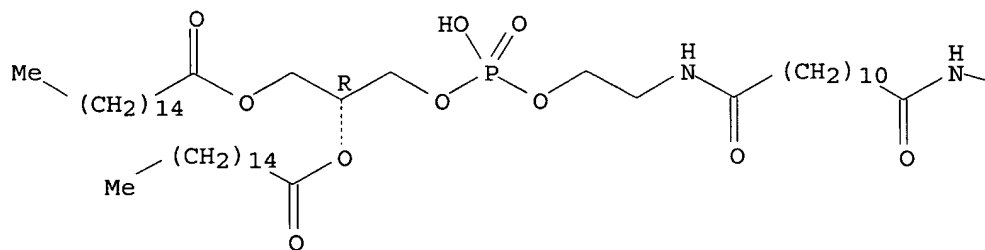
(targeting moiety; preparation of gas microsphere-liposome composites for delivery of diagnostic and therapeutic agents)

RN 250612-24-9 HCAPLUS

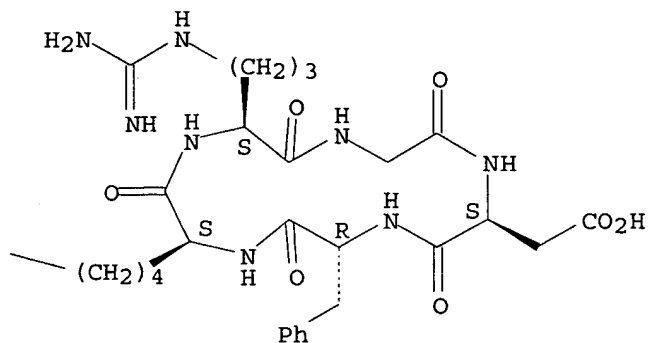
CN Cyclo[L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-N6-[(20R)-17-hydroxy-17-oxido-1,12,23-trioxo-20-[(1-oxohexadecyl)oxy]-16,18,22-trioxa-13-aza-17-phosphaoctatriacont-1-yl]-L-lysyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



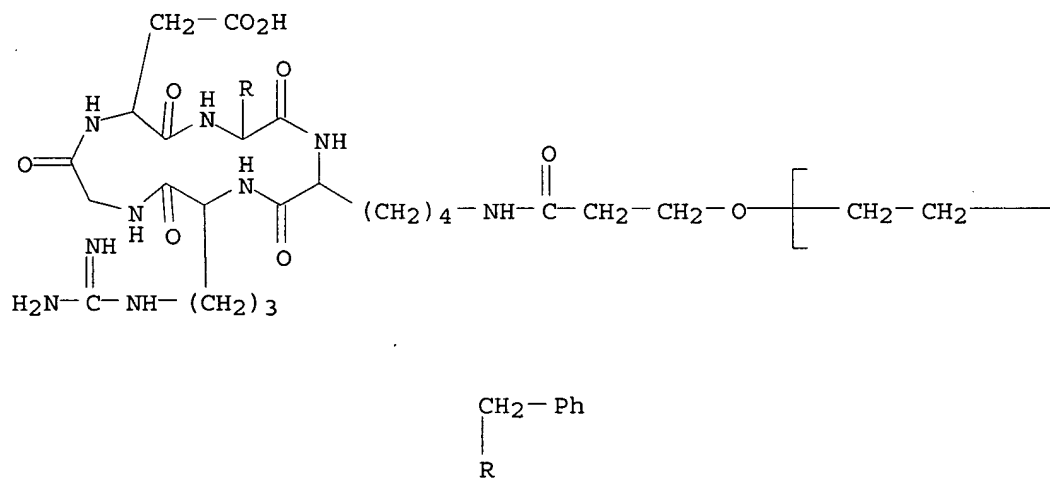
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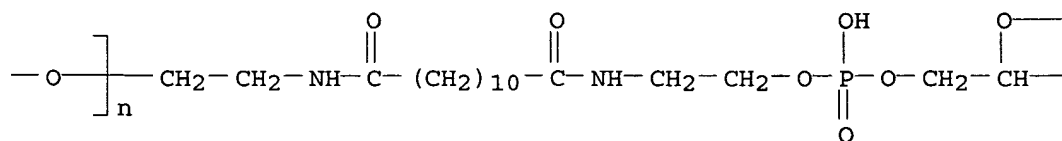
RN 250612-25-0 HCAPLUS

CN Cyclo[L-arginylglycyl-L-α-aspartyl-D-phenylalanyl-N6-(3-hydroxy-1-oxopropyl)-L-lysyl], ether with α-[(23R)-20-hydroxy-20-oxido-4,15,26-trioxo-23-[(1-oxohexadecyl)oxy]-19,21,25-trioxa-3,16-diaza-20-phosphahentriacont-1-yl]-ω-hydroxypoly(oxy-1,2-ethanediyl) (9CI)
(CA INDEX NAME)

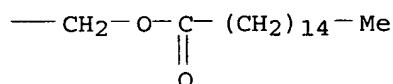
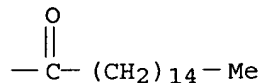
PAGE 1-A



PAGE 1-B



PAGE 1-C



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 34 OF 43 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:88158 HCAPLUS

DOCUMENT NUMBER: 139:272951

TITLE: Comparison of a monomeric and dimeric radiolabeled RGD-peptide for tumor targeting

AUTHOR(S): Janssen, Marcel; Oyen, Wim J. G.; Massuger, Leon F. A. G.; Frielink, Cathelijne; Dijkgraaf, Ingrid; Edwards, D. Scott; Radjopadhye, Milind; Corstens, Frans H. M.; Boerman, Otto C.

CORPORATE SOURCE: Department of Nuclear Medicine, Obstetrics and Gynecology, University Medical Center Nijmegen, Nijmegen, Neth.

SOURCE: Cancer Biotherapy & Radiopharmaceuticals (2002), 17(6), 641-646

CODEN: CBRAFJ; ISSN: 1084-9785

PUBLISHER: Mary Ann Liebert, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The $\alpha\text{v}\beta 3$ **integrin**, a transmembrane heterodimeric protein expressed on sprouting endothelial cells, binds to the arginine-glycine-aspartic acid (RGD) amino acid sequence of extracellular matrix proteins such as vitronectin. Growing malignant tumors continuously require angiogenesis. As a result, $\alpha\text{v}\beta 3$ is preferentially expressed in growing tumors and is a potential target for radiolabeled RGD-peptides. In this study we compared the tumor targeting characteristics of a monomeric radiolabeled RGD-peptide with those of a dimeric analog. Both peptides were radiolabeled with $^{99\text{m}}\text{Tc}$ via the hydrazinonicotinamid (=HYNIC) moiety to form $^{99\text{m}}\text{Tc}$ -HYNIC-c(RGDfK) and $^{99\text{m}}\text{Tc}$ -HYNIC-E-[c(RGDfK)]₂. In vitro, the IC₅₀ showed a 10 fold higher affinity of the dimer for the $\alpha\text{v}\beta 3$ **integrin** as compared to the monomer (0.1 vs. 1.0 nM). In a thymic female BALB/c mice with s.c. growing OVCAR-3 ovarian carcinoma **xenografts**, tumor uptake peaked at 5.8 ± 0.7 %ID/g and 5.2 ± 0.6 %ID/g for the dimer and the monomer, resp. At 1, 2, and 4 h postinjection (p.i.) uptake of the dimer in the tumor was significantly higher than that of the monomeric analog. Tumor-to-blood ratios were highest at 24 h p.i. at a value of 63 for both compds. At all timepoints kidney retention of the dimer was significantly higher as compared to kidney retention of the monomer. In conclusion, in this mouse model the dimeric RGD-peptide showed better retention in the tumor than the monomeric analog, most likely due to the bivalent interaction with the target cell. Furthermore, kidney retention of the dimeric peptide was higher than that of the monomeric peptide.

CC 8-9 (Radiation Biochemistry)

IT Ovary, neoplasm
(carcinoma; comparison of monomeric and dimeric radiolabeled RGD-peptide for targeting $\alpha\beta 3$ **integrin** expressing ovarian carcinoma and its retention in kidney)

IT Antitumor agents
Kidney
(comparison of monomeric and dimeric radiolabeled RGD-peptide for targeting $\alpha\beta 3$ **integrin** expressing ovarian carcinoma and its retention in kidney)

IT Carcinoma
(ovarian; comparison of monomeric and dimeric radiolabeled RGD-peptide for targeting $\alpha\beta 3$ **integrin** expressing ovarian carcinoma and its retention in kidney)

IT Radiotherapy
(targeted; comparison of monomeric and dimeric radiolabeled RGD-peptide for targeting $\alpha\beta 3$ **integrin** expressing ovarian carcinoma and its retention in kidney)

IT **Integrins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
($\alpha\beta 3$; comparison of monomeric and dimeric radiolabeled RGD-peptide for targeting $\alpha\beta 3$ **integrin** expressing ovarian carcinoma and its retention in kidney)

IT 250614-52-9 250614-55-2
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(comparison of monomeric and dimeric radiolabeled RGD-peptide for targeting $\alpha\beta 3$ **integrin** expressing ovarian carcinoma and its retention in kidney)

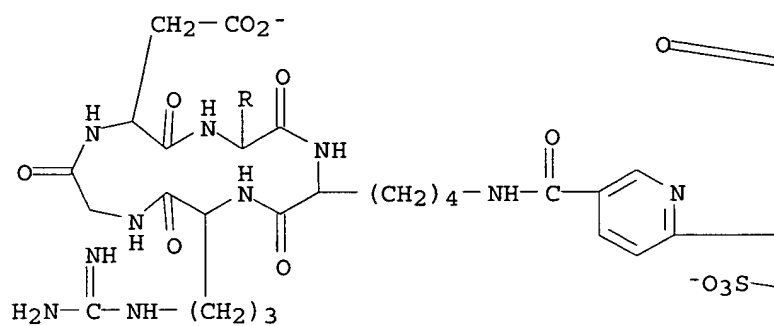
IT 250614-52-9 250614-55-2
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(comparison of monomeric and dimeric radiolabeled RGD-peptide for targeting $\alpha\beta 3$ **integrin** expressing ovarian carcinoma and its retention in kidney)

IT 250614-52-9 250614-55-2
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(comparison of monomeric and dimeric radiolabeled RGD-peptide for targeting $\alpha\beta 3$ **integrin** expressing ovarian carcinoma and its retention in kidney)

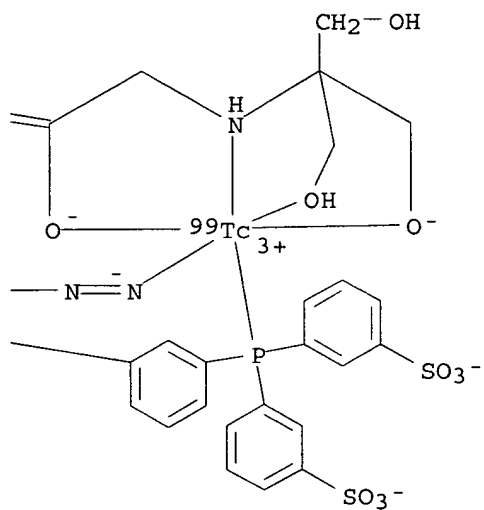
RN 250614-52-9 HCAPLUS

CN Technetate(4-)-99Tc, [cyclo[L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-N6-[[6-(diazenyl- κ N2)-3-pyridinyl]carbonyl]-L-lysylato(2-)]][N-[2-hydroxy-1,1-bis[(hydroxy- κ O)methyl]ethyl]glycina to(2-)- κ N, κ O][[3,3',3''-(phosphinidyne- κ P)tris[benzenesulfonato]](3-)]-, trisodium hydrogen (9CI) (CA INDEX NAME)

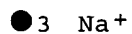
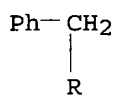
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PAGE 1-B

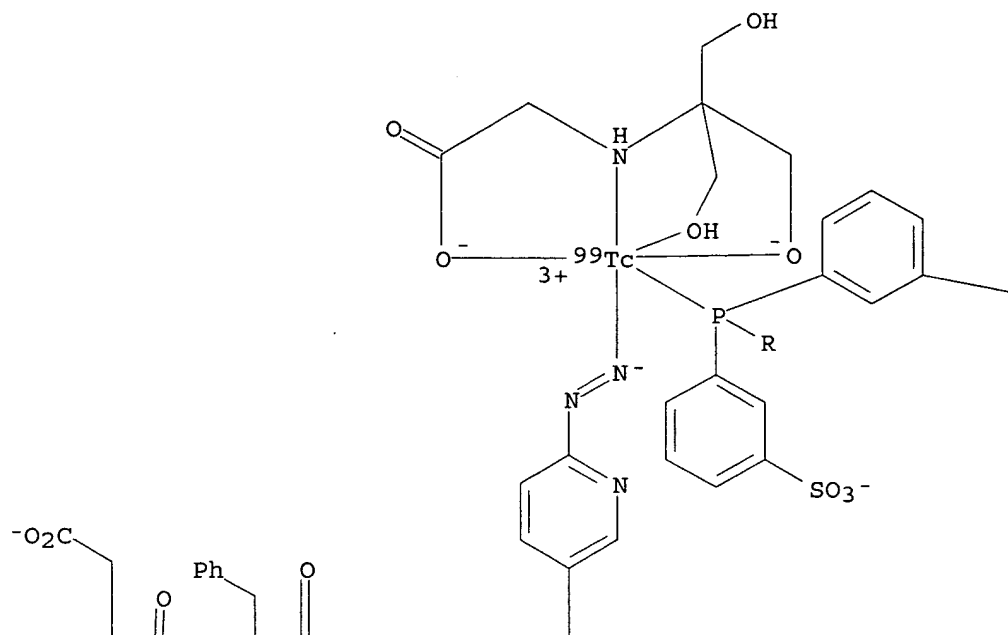


PAGE 2-A

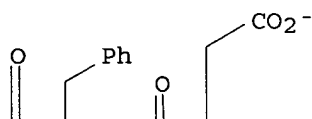
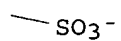


CN Technetate(5-)-⁹⁹Tc, [[5,5'-[N-[6-(diazenyl-κN2)-3-pyridinyl]carbonyl]-L-glutamoyl]bis[cyclo(L-arginylglycyl-L-α-aspartyl-D-phenylalanyl-L-lysylato)]](3-)] [N-[2-hydroxy-1,1-bis[(hydroxy-κO)methyl]ethyl]glycinato(2-)-κN,κO][[3,3',3''-(phosphinidyne-κP)tris[benzenesulfonato]](3-)]-, trisodium dihydrogen (9CI) (CA INDEX NAME)

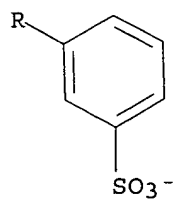
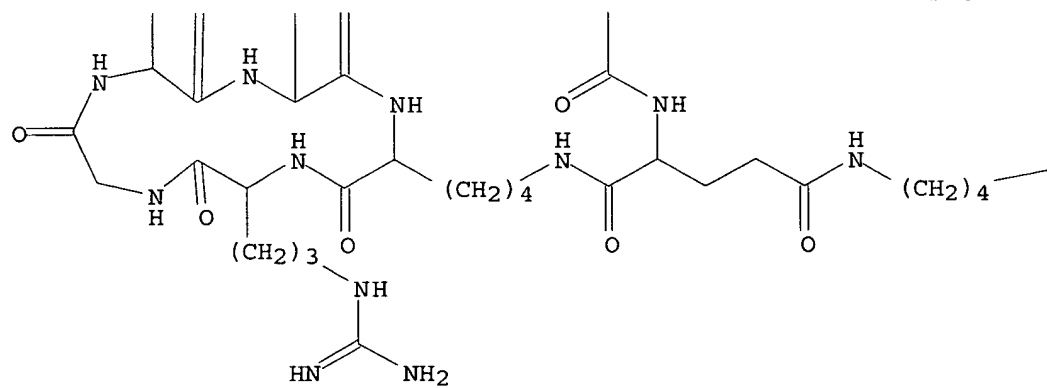
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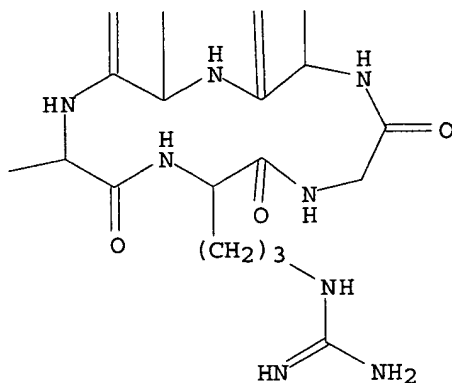
PAGE 1-B



PAGE 2-A



PAGE 2-B

● 2 H⁺● 3 Na⁺

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 35 OF 43 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:859512 HCAPLUS

DOCUMENT NUMBER: 138:316851

TITLE: Tumor targeting with radiolabeled $\alpha\beta 3$ **integrin** binding peptides in a nude mouse model

AUTHOR(S): Janssen, Marcel L.; Oyen, Wim J.; Dijkgraaf, Ingrid; Massuger, Leon F.; Frielink, Cathelijne; Edwards, D. Scott; Rajopadhye, Milind; Boonstra, Henk; Corstens, Frans H.; Boerman, Otto C.

CORPORATE SOURCE: Departments of Nuclear Medicine and Obstetrics and Gynecology, University Medical Center Nijmegen, Nijmegen, 6500 HB, Neth.

SOURCE: Cancer Research (2002), 62(21), 6146-6151
CODEN: CNREA8; ISSN: 0008-5472

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

LANGUAGE: English

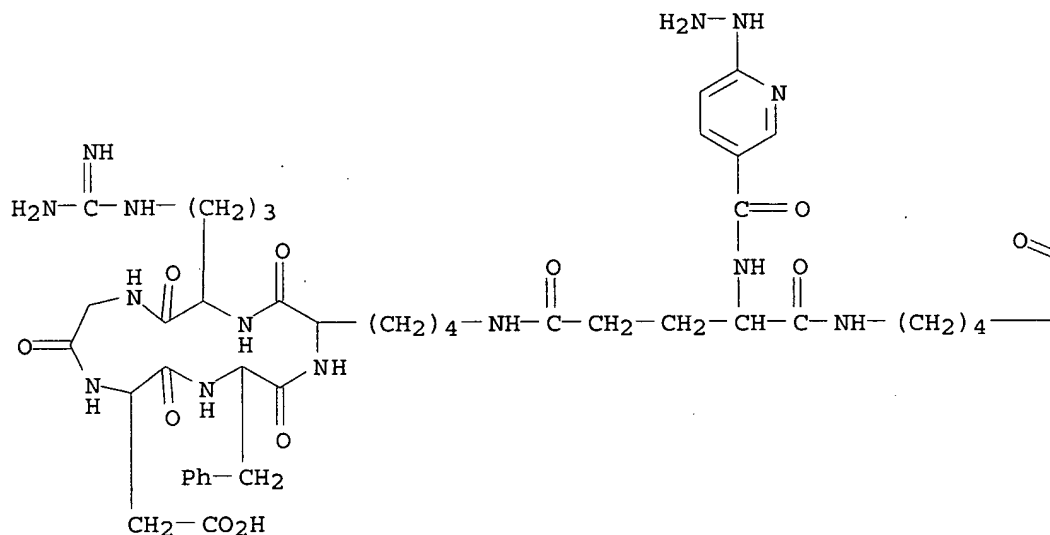
AB The $\alpha\beta 3$ **integrin** is expressed on proliferating endothelial cells such as those present in growing tumors, as well as on tumor cells of various origin. Tumor-induced angiogenesis can be blocked in vivo by antagonizing the $\alpha\beta 3$ **integrin** with small peptides containing the Arg-Gly-Asp (RGD) amino acid sequence. This tripeptidic sequence, naturally present in extracellular matrix proteins, is the primary binding site of the $\alpha\beta 3$ **integrin**. Because of selective expression of $\alpha\beta 3$ **integrin** in tumors, radiolabeled RGD peptides are attractive candidates for $\alpha\beta 3$ **integrin** targeting in tumors. We studied the in vivo behavior of the radiolabeled dimeric RGD peptide E-[c(RGDfK)]₂ in the NIH:OVCAR-3 s.c. ovarian carcinoma **xenograft** model in BALB/c nude mice. Conjugation of the 1,4,7,10-tetraazadodecane-N,N',N'',N'''-tetraacetic acid (DOTA) and hydrazinonicotinamide (HYNIC) chelators enabled efficient radiolabeling with ¹¹¹In/90Y and ^{99m}Tc, resp. The radiolabeled peptide was rapidly excreted renally. Uptake in nontarget organs such as liver and spleen was considerable. Tumor uptake peaked at 7.5% injected dose (ID)/g (¹¹¹In-DOTA-E-[c(RGDfK)]₂) or 6.0% ID/g (^{99m}Tc-HYNIC-E-[c(RGDfK)]₂) at 2 and 1 h postinjection, resp. **Integrin** $\alpha\beta 3$ receptor binding specificity was demonstrated by reduced tumor uptake after injection of the scrambled

control peptide ^{111}In -DOTA-E-[c(RGDfD)]₂ (0.28% ID/g at 2 h p.i.) and after coinjection of excess nonradioactive ^{115}In -DOTA-E-[c(RGDfK)]₂ (0.22% ID/g at 2 h p.i.). A single injection of ^{90}Y -DOTA-E-[c(RGDfK)]₂ at the maximum-tolerated dose (37 MBq) in mice with small s.c. tumors caused a significant growth delay as compared with mice treated with 37 MBq ^{90}Y -labeled scrambled peptide or untreated mice (median survival of 54 vs. 33.5 vs. 19 days, resp.). In conclusion, the radiolabeled RGD peptides ^{111}In -DOTA-E-[c(RGDfK)]₂ and $^{99\text{mTc}}$ -HYNIC-E-[c(RGDfK)]₂ demonstrated high and specific tumor uptake in a human tumor **xenograft**. Injection of ^{90}Y -DOTA-E-[c(RGDfK)]₂ induced a significant delay in tumor growth. Potentially, these peptides can be used for peptide receptor radionuclide imaging as well as therapy.

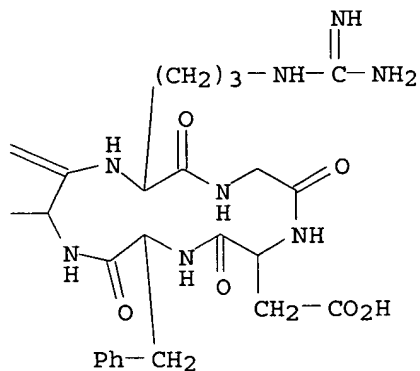
- CC 8-9 (Radiation Biochemistry)
- ST ovarian carcinoma targeting radiolabeled **integrin** binding peptide biodistribution antitumor; antitumor indium 111 yttrium 90 technetium 99 peptide **integrin**; angiogenesis antitumor radiolabeled **integrin** binding peptide
- IT Ovary, neoplasm
(carcinoma; tumor targeting with radiolabeled $\alpha\text{v}\beta 3$ **integrin**-binding peptides: biodistribution and antitumor action)
- IT Peptides, biological studies
RL: DGN (Diagnostic use); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(labeled; tumor targeting with radiolabeled $\alpha\text{v}\beta 3$ **integrin**-binding peptides: biodistribution and antitumor action)
- IT Carcinoma
(ovarian; tumor targeting with radiolabeled $\alpha\text{v}\beta 3$ **integrin**-binding peptides: biodistribution and antitumor action)
- IT RGD peptides
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(radiolabeled; tumor targeting with radiolabeled $\alpha\text{v}\beta 3$ **integrin**-binding peptides: biodistribution and antitumor action)
- IT Angiogenesis inhibitors
Antitumor agents
Drug delivery systems
Human
Imaging agents
Radiotherapy
Scintigraphy
(tumor targeting with radiolabeled $\alpha\text{v}\beta 3$ **integrin** -binding peptides: biodistribution and antitumor action)
- IT **Integrins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
($\alpha\text{v}\beta 3$; tumor targeting with radiolabeled $\alpha\text{v}\beta 3$ **integrin**-binding peptides: biodistribution and antitumor action)
- IT 14133-76-7D, $^{99\text{Tc}}$, complex with cyclic peptides, biological studies
500166-11-0D, complex with Tc- $^{99\text{m}}$ **514172-04-4**
RL: DGN (Diagnostic use); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tumor targeting with radiolabeled $\alpha\text{v}\beta 3$ **integrin** -binding peptides: biodistribution and antitumor action)
- IT **514172-05-5**
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(tumor targeting with radiolabeled $\alpha\text{v}\beta 3$ **integrin**
 -binding peptides: biodistribution and antitumor action)
 IT 500166-11-0D, complex with Tc-99m 514172-04-4
 RL: DGN (Diagnostic use); PKT (Pharmacokinetics); THU (Therapeutic use);
 BIOL (Biological study); USES (Uses)
 (tumor targeting with radiolabeled $\alpha\text{v}\beta 3$ **integrin**
 -binding peptides: biodistribution and antitumor action)
 IT 514172-05-5
 RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU
 (Therapeutic use); BIOL (Biological study); USES (Uses)
 (tumor targeting with radiolabeled $\alpha\text{v}\beta 3$ **integrin**
 -binding peptides: biodistribution and antitumor action)
 IT 500166-11-0D, complex with Tc-99m 514172-04-4
 RL: DGN (Diagnostic use); PKT (Pharmacokinetics); THU (Therapeutic use);
 BIOL (Biological study); USES (Uses)
 (tumor targeting with radiolabeled $\alpha\text{v}\beta 3$ **integrin**
 -binding peptides: biodistribution and antitumor action)
 RN 500166-11-0 HCAPLUS
 CN Cyclo(L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-L-lysyl),
 5,5'-[N-[(6-hydrazino-3-pyridinyl)carbonyl]-L-glutamoyl]bis- (9CI) (CA
 INDEX NAME)

PAGE 1-A

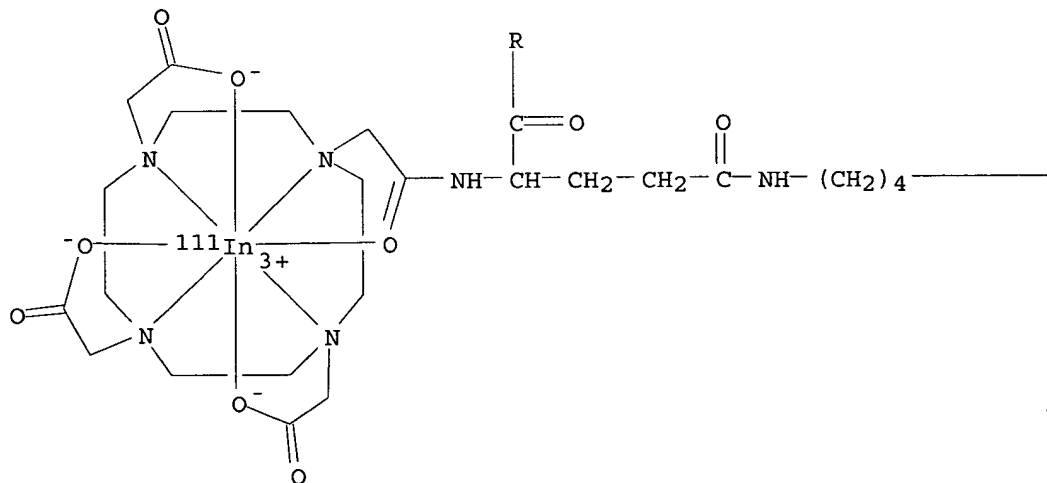


PAGE 1-B

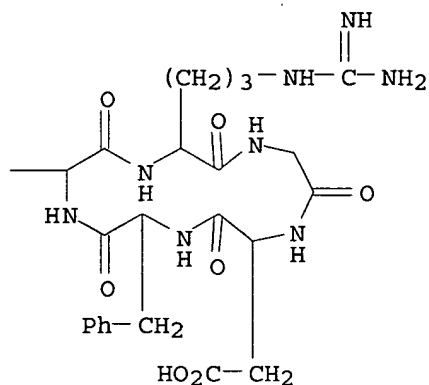


RN 514172-04-4 HCAPLUS
 CN Indium-111In, [[5,5'-[N-[[4,7,10-tris[(carboxy- κO)methyl]-1,4,7,10-tetraazacyclododec-1-yl- $\kappa\text{N1},\kappa\text{N4},\kappa\text{N7},\kappa\text{N10}$]acetyl- κO]-L-glutamoyl]bis[cyclo(L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-L-lysylato)]](3-)]- (9CI) (CA INDEX NAME)

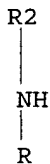
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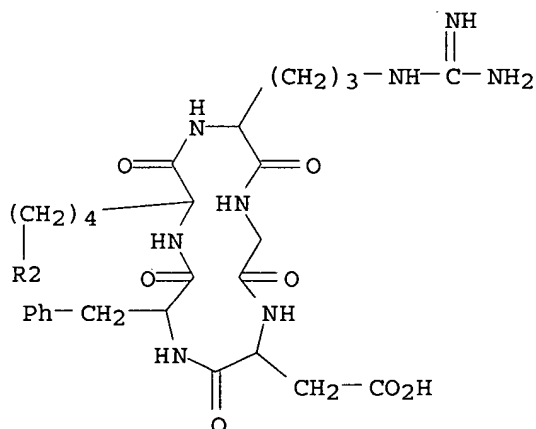
PAGE 1-B



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PAGE 3-A



IT 514172-05-5

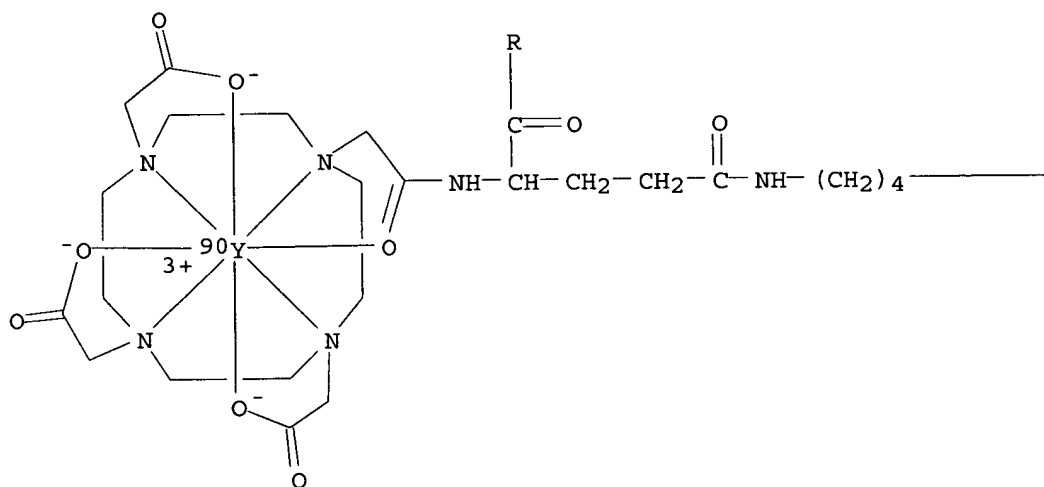
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU
(Therapeutic use); BIOL (Biological study); USES (Uses)
(tumor targeting with radiolabeled $\alpha\text{v}\beta 3$ **integrin**
-binding peptides: biodistribution and antitumor action)

RN 514172-05-5 HCAPLUS

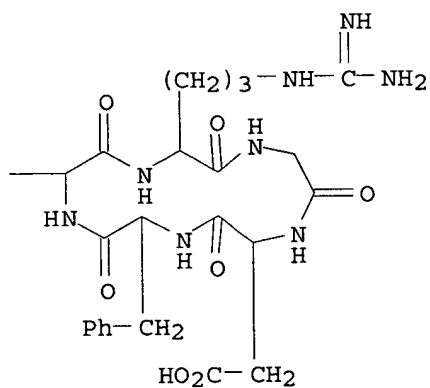
CN Yttrium-90Y, [[5,5'-[N-[[4,7,10-tris[(carboxy- κO)methyl]-1,4,7,10-
tetraazacyclododec-1-yl- $\kappa\text{N}1,\kappa\text{N}4,\kappa\text{N}7,\kappa\text{N}10$]acetyl-
 κO]-L-glutamoyl]bis[cyclo(L-arginylglycyl-L- α -aspartyl-D-

phenylalanyl-L-lysylato)](3-)]- (9CI) (CA INDEX NAME)

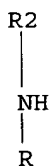
PAGE 1-A



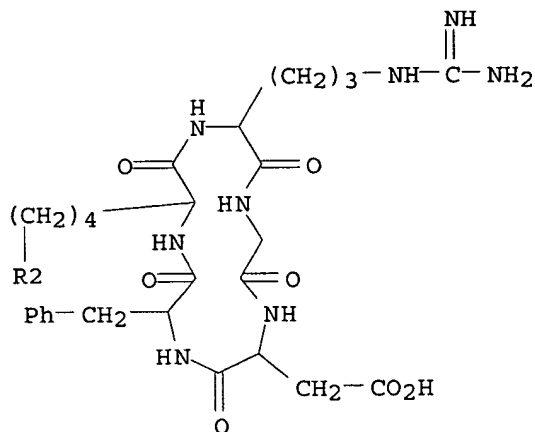
PAGE 1-B



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PAGE 3-A



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 36 OF 43 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:336940 HCAPLUS

DOCUMENT NUMBER: 138:250879

TITLE: Decorated surfaces by biofunctionalized gold beads: application to cell adhesion studies

AUTHOR(S): Abdelghani-Jacquín, C.; Abdelghani, A.; Chmel, G.; Kantlehner, M.; Sackmann, E.

CORPORATE SOURCE: Physik Department, Technische Universität München, Institut für Biophysik E22, Garching, 85747, Germany

SOURCE: European Biophysics Journal (2002), 31(2), 102-110
CODEN: EBJOE8; ISSN: 0175-7571

PUBLISHER: Springer-Verlag

DOCUMENT TYPE: Journal

LANGUAGE: English

AB We describe a simple but versatile method to decorate solid surfaces randomly with colloidal gold particles to which ligands of cell receptors can be coupled to generate local attraction sites for the control of cell adhesion. A self-assembled monolayer of (3-mercaptopropyl)trimethoxysilane was deposited on glass slides. Gold beads were anchored to the functionalized surface through the sulfur group. We characterized the gold bead distribution on the functionalized surface with reflection interference contrast microscopy. The gold beads were functionalized with a disulfide-coupled cyclic pentapeptide containing an arginine-glycine-aspartic acid (RGD) tripeptide sequence which is selectively recognized by **integrin** receptors $\alpha V\beta 3$ of endothelial cells. A blocking layer of bovine serum albumin was adsorbed onto the surface to prevent non-specific binding of the cells. We demonstrate that the RGD-functionalized colloidal gold beads act as local attraction centers, mediating rapid cell anchoring on a substrate impeding cell adhesion in the absence of attraction centers. Surprisingly, microinterferometry shows that after a time delay of about 1 h, the regions of the cell surface between the gold beads form close contacts with the substrate, which is attributed to strong van der Waals attraction after escape of repeller mols. from the contact surface.

CC 9-4 (Biochemical Methods)

IT Adhesion, biological

(cell; method for generation of biofunctionalized gold beads coupled to

- disulfide cyclic peptides on surface-**grafted** monolayers for cell adhesion studies)
- IT Microscopy
Self-assembled monolayers
Sulfhydryl group
Van der Waals force
(method for generation of biofunctionalized gold beads coupled to disulfide cyclic peptides on surface-**grafted** monolayers for cell adhesion studies)
- IT **Integrins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(method for generation of biofunctionalized gold beads coupled to disulfide cyclic peptides on surface-**grafted** monolayers for cell adhesion studies)
- IT Albumins, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(serum; method for generation of biofunctionalized gold beads coupled to disulfide cyclic peptides on surface-**grafted** monolayers for cell adhesion studies)
- IT **Integrins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
($\alpha\beta 3$; method for generation of biofunctionalized gold beads coupled to disulfide cyclic peptides on surface-**grafted** monolayers for cell adhesion studies)
- IT 7440-57-5, Gold, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(beads, coupled to disulfide-coupled cyclic peptide; method for generation of biofunctionalized gold beads coupled to disulfide cyclic peptides on surface-**grafted** monolayers for cell adhesion studies)
- IT **502634-66-4P**
RL: BUU (Biological use, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(method for generation of biofunctionalized gold beads coupled to disulfide cyclic peptides on surface-**grafted** monolayers for cell adhesion studies)
- IT 1077-28-7, 1,2-Dithiolane-3-pentanoic acid **339547-54-5**
RL: RCT (Reactant); RACT (Reactant or reagent)
(method for generation of biofunctionalized gold beads coupled to disulfide cyclic peptides on surface-**grafted** monolayers for cell adhesion studies)
- IT **502634-65-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(method for generation of biofunctionalized gold beads coupled to disulfide cyclic peptides on surface-**grafted** monolayers for cell adhesion studies)
- IT 4420-74-0, (3-Mercaptopropyl)trimethoxysilane
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(monolayer; method for generation of biofunctionalized gold beads coupled to disulfide cyclic peptides on surface-**grafted** monolayers for cell adhesion studies)
- IT **502634-66-4P**
RL: BUU (Biological use, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(method for generation of biofunctionalized gold beads coupled to disulfide cyclic peptides on surface-**grafted** monolayers for

cell adhesion studies)

IT 339547-54-5

RL: RCT (Reactant); RACT (Reactant or reagent)
(method for generation of biofunctionalized gold beads coupled to disulfide cyclic peptides on surface-**grafted** monolayers for cell adhesion studies)

IT 502634-65-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(method for generation of biofunctionalized gold beads coupled to disulfide cyclic peptides on surface-**grafted** monolayers for cell adhesion studies)

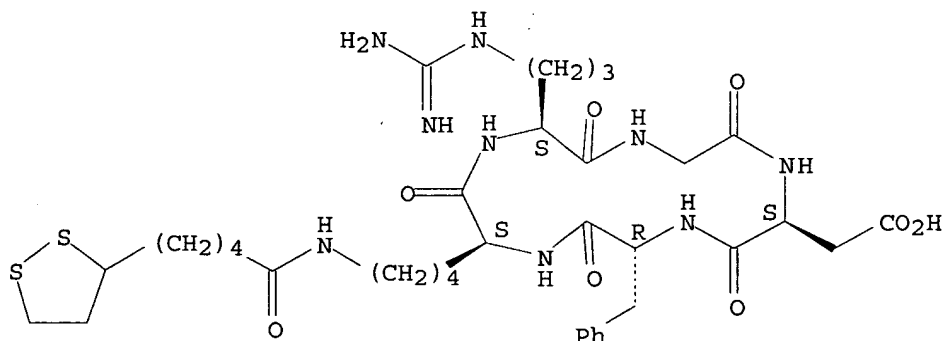
IT 502634-66-4P

RL: BUU (Biological use, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(method for generation of biofunctionalized gold beads coupled to disulfide cyclic peptides on surface-**grafted** monolayers for cell adhesion studies)

RN 502634-66-4 HCAPLUS

CN Cyclo[L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-N6-[5-(1,2-dithiolan-3-yl)-1-oxopentyl]-L-lysyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 339547-54-5

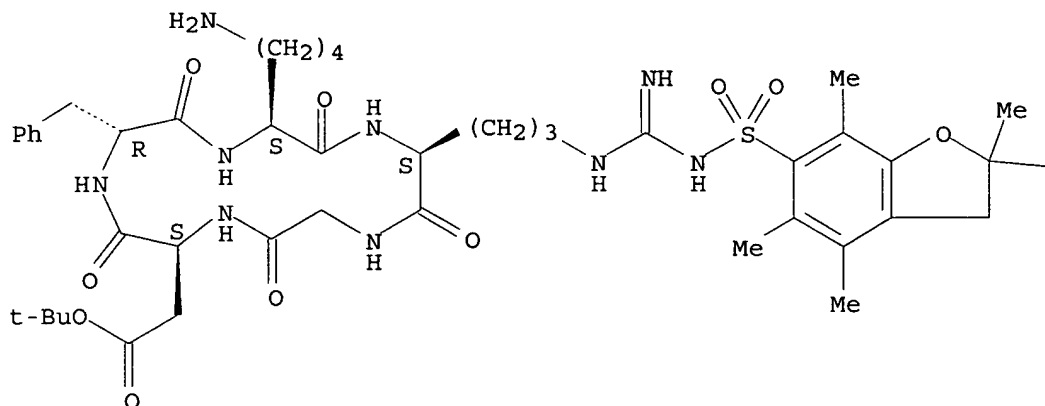
RL: RCT (Reactant); RACT (Reactant or reagent)
(method for generation of biofunctionalized gold beads coupled to disulfide cyclic peptides on surface-**grafted** monolayers for cell adhesion studies)

RN 339547-54-5 HCAPLUS

CN Cyclo[L- α -aspartyl-D-phenylalanyl-L-lysyl-N5-[[[(2,3-dihydro-2,2,4,5,7-pentamethyl-6-benzofuranyl)sulfonyl]amino]iminomethyl]-L-ornithyl], 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

— Me

IT 502634-65-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

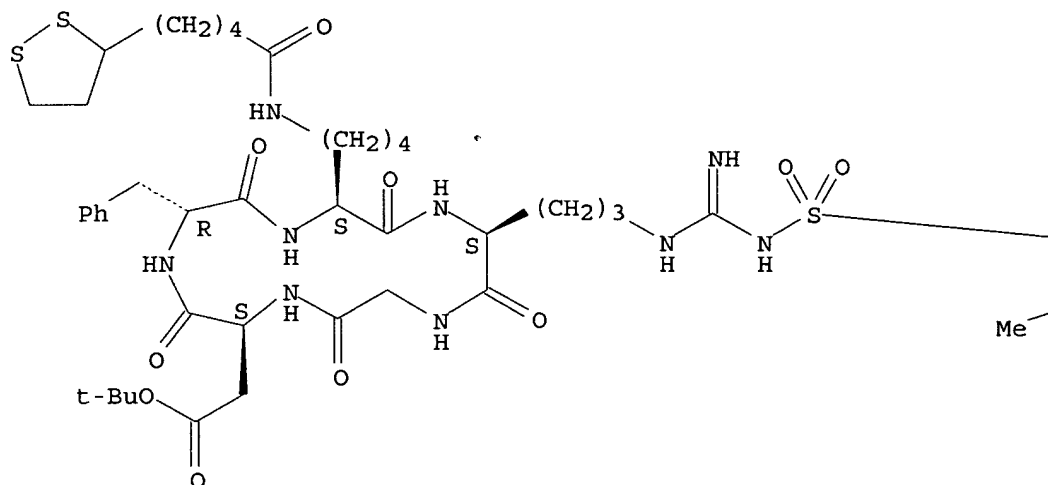
(method for generation of biofunctionalized gold beads coupled to disulfide cyclic peptides on surface-grafted monolayers for cell adhesion studies)

RN 502634-65-3 HCAPLUS

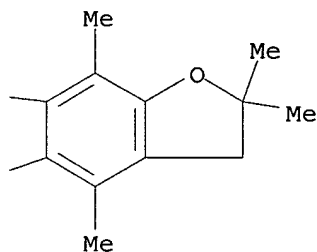
CN Cyclo[L-α-aspartyl-D-phenylalanyl-N6-[5-(1,2-dithiolan-3-yl)-1-oxopentyl]-L-lysyl-N5-[[[(2,3-dihydro-2,2,4,5,7-pentamethyl-6-benzofuranyl)sulfonyl]amino]iminomethyl]-L-ornithylglycyl], 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 37 OF 43 HCAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2002:51305 HCAPLUS
 DOCUMENT NUMBER: 136:123597
 TITLE: Preparation of stable radiopharmaceutical compositions useful for tumor therapy
 INVENTOR(S): Liu, Shuang; Barrett, John A.; Carpenter, Alan P., Jr.
 PATENT ASSIGNEE(S): Dupont Pharmaceuticals Company, USA
 SOURCE: PCT Int. Appl., 127 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2002004030      A2      20020117      WO 2001-US21261      20010705
WO 2002004030      A3      20030227
W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
    CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
    HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
    LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
    SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU,
    ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
    DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
    BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
CA 2413538          AA      20020117      CA 2001-2413538      20010705
US 2002122768       A1      20020905      US 2001-899629      20010705
EP 1311301          A2      20030521      EP 2001-984147      20010705
R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
    IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
PRIORITY APPLN. INFO.:      US 2000-216396P      P 20000706
                                WO 2001-US21261      W 20010705

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OTHER SOURCE(S): MARPAT 136:123597

AB The present invention provides stable radiopharmaceutical compns. including a therapeutic radionuclide and an effective stabilizing amount of an aromatic stabilizer (e.g., a polyhydroxylated aromatic compound, an aromatic amine, or a hydroxylated aromatic amine), alone or in combination with other antioxidants or stabilizers, to inhibit radiolytic degradation of radiopharmaceuticals. The present invention also provides improved radiopharmaceutical formulations by the use of an aromatic stabilizing agent (e.g., a polyhydroxylated aromatic compound, an aromatic amines, or a hydroxylated

aromatic amine), and/or low temperature storage. The present invention also provides processes for making stable radiopharmaceutical compns. The present invention also provides the use of the pharmaceutical compns. in medical therapy and/or medical diagnosis.

IC ICM A61K051-04

ICS A61K051-08

CC 63-5 (Pharmaceuticals)

Section cross-reference(s): 8, 34, 78

IT Epidermal growth factor receptors

Fibrinogen receptors

Growth factor receptors

Integrins

RL: BSU (Biological study, unclassified); BIOL (Biological study) (disease associated with; stabilized radiopharmaceutical compns. for use in medical therapy and/or medical diagnosis)

IT Integrins

RL: BSU (Biological study, unclassified); BIOL (Biological study) (α IIb β 3, disease associated with; stabilized radiopharmaceutical compns. for use in medical therapy and/or medical diagnosis)

IT Integrins

Integrins

RL: BSU (Biological study, unclassified); BIOL (Biological study) (α v β 3, disease associated with; stabilized radiopharmaceutical compns. for use in medical therapy and/or medical diagnosis)

IT Integrins

RL: BSU (Biological study, unclassified); BIOL (Biological study) (α v β 5, disease associated with; stabilized radiopharmaceutical compns. for use in medical therapy and/or medical diagnosis)

IT Integrins

RL: BSU (Biological study, unclassified); BIOL (Biological study)

($\alpha 1\beta 1$, disease associated with; stabilized radiopharmaceutical compns. for use in medical therapy and/or medical diagnosis)

IT **Integrins**

RL: BSU (Biological study, unclassified); BIOL (Biological study)
($\alpha 4\beta 1$, disease associated with; stabilized radiopharmaceutical compns. for use in medical therapy and/or medical diagnosis)

IT **Integrins****Integrins**

RL: BSU (Biological study, unclassified); BIOL (Biological study)
($\alpha 5\beta 1$, disease associated with; stabilized radiopharmaceutical compns. for use in medical therapy and/or medical diagnosis)

IT 50-07-7, Mitomycin 57-22-7, Vincristine 57-83-0, Progesterone, biological studies 59-05-2, Methotrexate 125-84-8, Aminoglutethimide 147-94-4, Cytarabine 302-79-4, Tretinoin 434-07-1, Oxymetholone 488-41-5, Mitobronitol 566-48-3, Formestane 2363-58-8, Epitiostanol 3094-09-5, Doxifluridine 3778-73-2, Ifosfamide 4291-63-8, Cladribine 4533-39-5, Nitracrine 4759-48-2, Isotretinoin 6620-60-6, Proglumide 9014-02-2, Zinostatin 9034-40-6, Lhrf 9050-67-3, Sizofilan 10318-26-0, Mitolactol 10540-29-1, Tamoxifen 13311-84-7, Flutamide 13425-98-4, Improsulfan 14769-73-4, Levamisole 17902-23-7, Tegafur 18016-80-3, Lisuride 18883-66-4, Streptozocin 20830-81-3, Daunorubicin 21362-69-6, Mepitiostane 21416-67-1, Razoxane 22181-94-8, Butocin 23214-92-8, **Doxorubicin** 24279-91-2, Carboquone 29069-24-7, Prednimustine 29767-20-2, Teniposide 33419-42-0, Etoposide 39325-01-4, Picibanil 41575-94-4, Carboplatin 42471-28-3, Nimustine 51264-14-3, Amsacrine 53643-48-4, Vindesine 53910-25-1, Pentostatin 54350-48-0, Etrretinate 55726-47-1, Enocitabine 58337-35-2, Elliptinium acetate 61422-45-5, Carmofur 62304-98-7, Thymalfasin 71486-22-1, Vinorelbine 74050-98-9, Ketanserin 81627-83-0, Colony stimulating factor-1 81840-15-5, Vesnarinone 83869-56-1, Colonystimulating factor-2 90357-06-5, Bicalutamide 92118-27-9, Fotemustine 95058-81-4, Gemcitabine 95734-82-0, Nedaplatin 98631-95-9, Sobuzoxane 102676-47-1, Fadrozole 112809-51-5, Letrozole 112887-68-0, Raltitrexed 120287-85-6, Cetorelix 173146-27-5, Denileukin diftitox
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chemotherapeutic agent; preparation of stable radiopharmaceutical compns. useful for tumor therapy)

IT 40324-66-1P 57932-18-0P **161552-03-0P** 246234-73-1P
250612-43-2P 250612-45-4P 250612-48-7P
250612-82-9P 277315-71-6P 277315-82-9P 277315-89-6P
277315-90-9P 277316-24-2P 277316-27-5P 277316-28-6P 277316-29-7P
277316-30-0P 277316-31-1P 277316-40-2P 277316-41-3P 277316-44-6P
277316-45-7P 277316-58-2P 389885-48-7DP, **oxime** resin-bound
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of chelator-optional linker-biomol. conjugates for use in stable radiopharmaceutical compns.)

IT **250612-07-8P** 277315-68-1P 277315-72-7P
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of chelator-optional linker-biomol. conjugates for use in stable radiopharmaceutical compns.)

IT **250614-38-1P** 278173-02-7P 278173-08-3P 390798-27-3P
RL: DGN (Diagnostic use); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of stable radiopharmaceutical compns. useful for tumor therapy)
IT **161552-03-0P 250612-43-2P 250612-45-4P**
250612-48-7P 250612-82-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

(Reactant or reagent)

(preparation of chelator-optional linker-biomol. conjugates for use in stable radiopharmaceutical compns.)

IT 250612-07-8P

RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of chelator-optional linker-biomol. conjugates for use in stable radiopharmaceutical compns.)

IT 250614-38-1P

RL: DGN (Diagnostic use); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of stable radiopharmaceutical compns. useful for tumor therapy)

IT 161552-03-0P 250612-43-2P 250612-45-4P

250612-48-7P 250612-82-9P

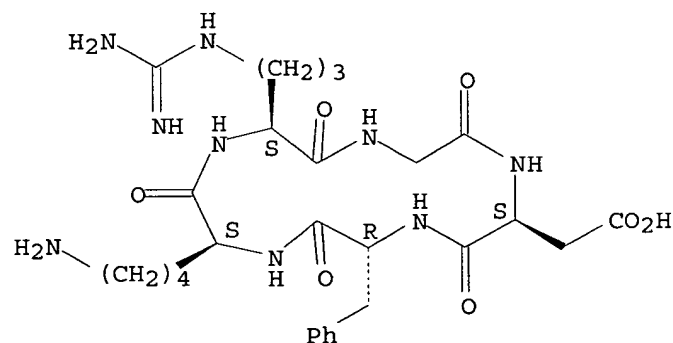
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of chelator-optional linker-biomol. conjugates for use in stable radiopharmaceutical compns.)

RN 161552-03-0 HCAPLUS

CN Cyclo(L-arginylglycyl-L-α-aspartyl-D-phenylalanyl-L-lysyl) (9CI)
(CA INDEX NAME)

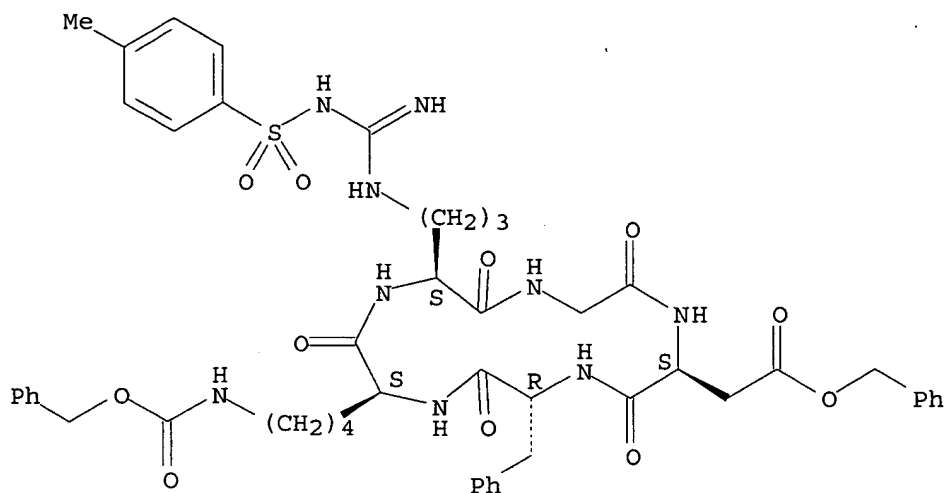
Absolute stereochemistry.



RN 250612-43-2 HCAPLUS

CN Cyclo[L-α-aspartyl-D-phenylalanyl-N6-[(phenylmethoxy)carbonyl]-L-lysyl-N5-[imino[[[4-methylphenyl)sulfonyl]amino]methyl]-L-ornithylglycyl], phenylmethyl ester (9CI) (CA INDEX NAME)

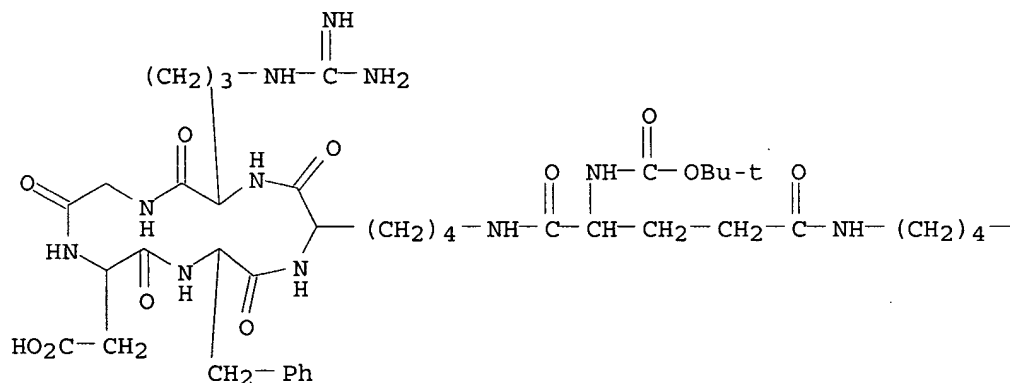
Absolute stereochemistry.



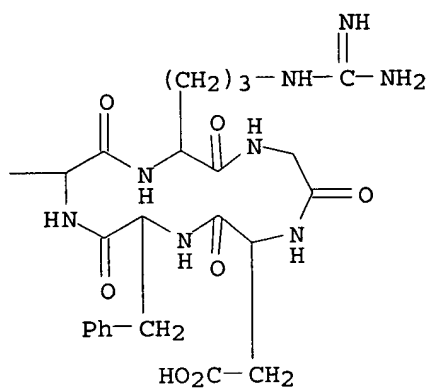
RN 250612-45-4 HCAPLUS

CN Cyclo(L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-L-lysyl),
5,5'-[N-[(1,1-dimethylethoxy)carbonyl]-L-glutamoyl]bis- (9CI) (CA INDEX
NAME)

PAGE 1-A



PAGE 1-B

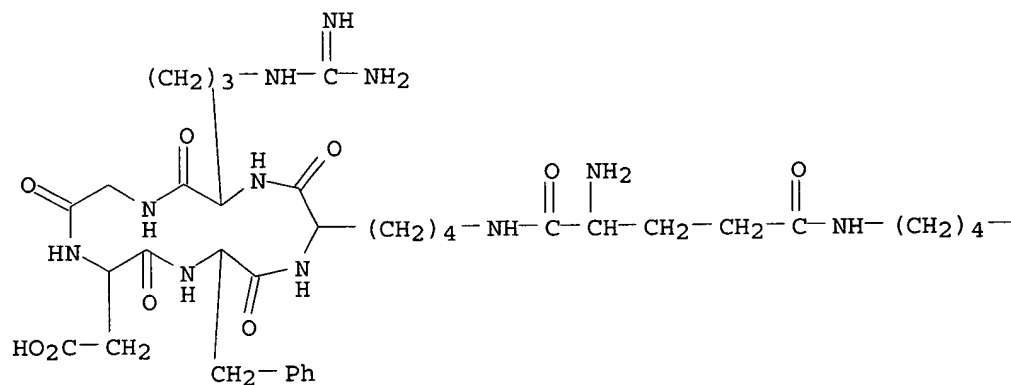


RN 250612-48-7 HCAPLUS
 CN Cyclo(L-arginylglycyl-L-α-aspartyl-D-phenylalanyl-L-lysyl),
 5,5'-L-glutamoylbis-, tris(trifluoroacetate) (9CI) (CA INDEX NAME)

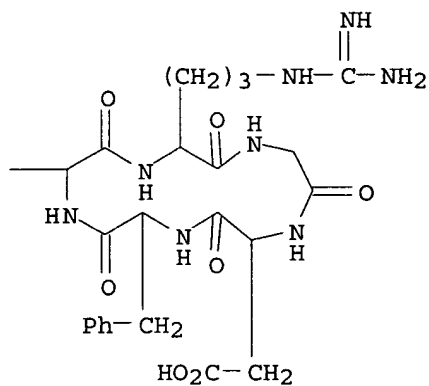
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CRN 250612-47-6
 CMF C59 H87 N19 O16

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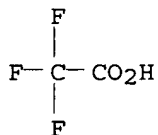
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CM 2

CRN 76-05-1

CMF C2 H F3 O2



RN 250612-82-9 HCAPLUS

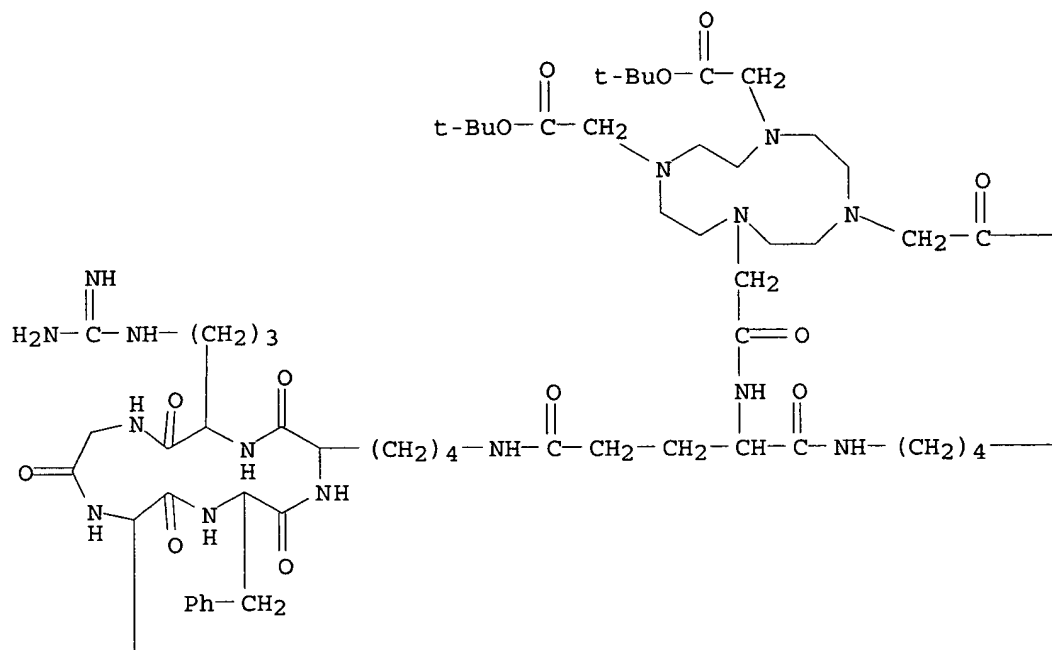
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 5,5'-[N-[[4,7,10-tris[2-(1,1-dimethylethoxy)-2-oxoethyl]-1,4,7,10-
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 (9CI) (CA INDEX NAME)

CM 1

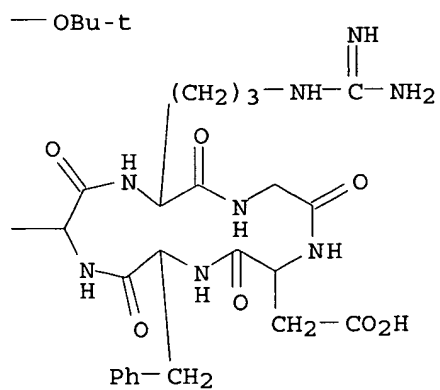
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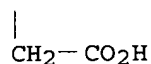
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PAGE 1-B



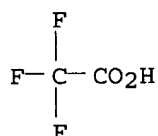
PAGE 2-A



CM 2

CRN 76-05-1

CMF C2 H F3 O2



IT 250612-07-8P

RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use);
 BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent);
 USES (Uses)

(preparation of chelator-optional linker-biomol. conjugates for use in
 stable radiopharmaceutical compns.)

RN 250612-07-8 HCAPLUS

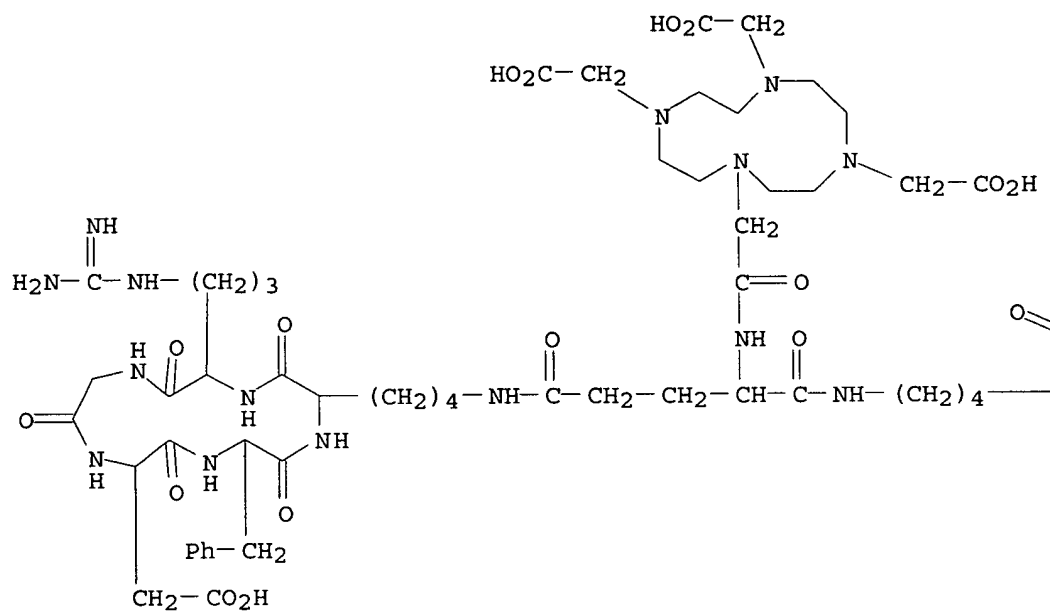
CN Cyclo(L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-L-lysyl),
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 yl]acetyl]-L-glutamoyl]bis-, bis(trifluoroacetate) (9CI) (CA INDEX NAME)

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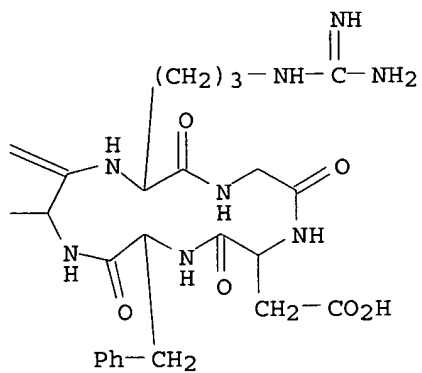
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CMF C75 H113 N23 O23

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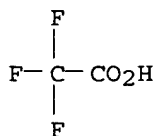
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CM 2

CRN 76-05-1

CMF C2 H F3 O2



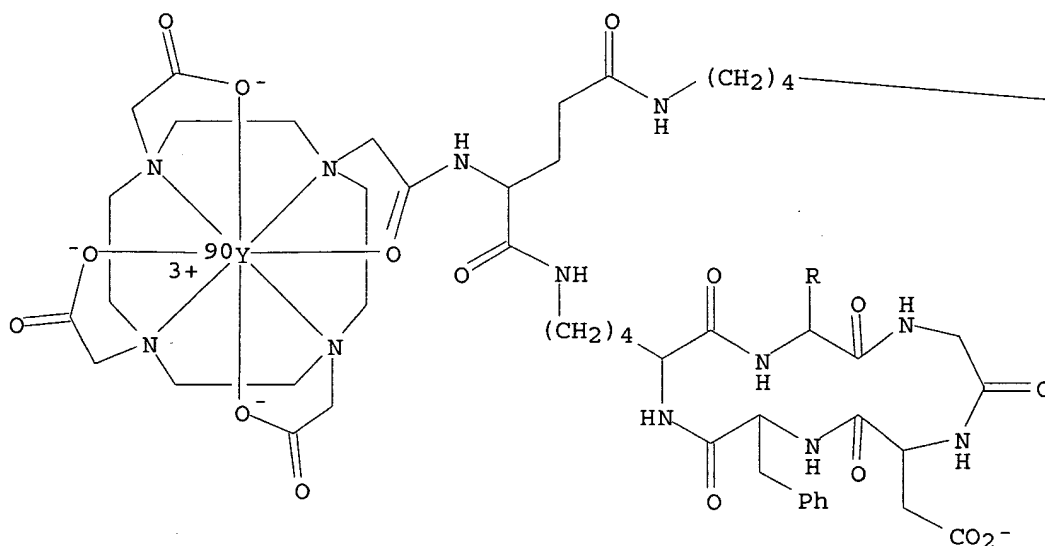
IT 250614-38-1P

RL: DGN (Diagnostic use); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of stable radiopharmaceutical compns. useful for tumor therapy)

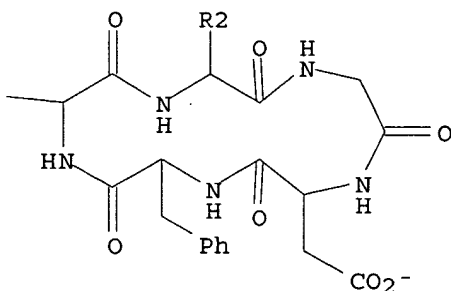
RN 250614-38-1 HCAPLUS

CN Yttrate(2-)-90Y, [[5,5'-[N-[[4,7,10-tris[(carboxy-κO)methyl]-1,4,7,10-tetraazacyclododec-1-yl-κN1,κN4,κN7,κN10]acetyl-κO]-L-glutamoyl]bis[cyclo(L-arginylglycyl-L-α-aspartyl-D-phenylalanyl-L-lysylato)]](5-)]-, dihydrogen (9CI) (CA INDEX NAME)

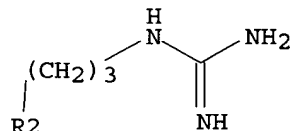
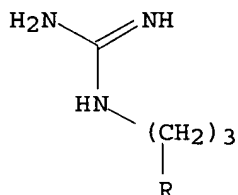
PAGE 1-A



PAGE 1-B



PAGE 2-A

● 2 H⁺

L47 ANSWER 38 OF 43 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:935453 HCAPLUS

DOCUMENT NUMBER: 136:54027

TITLE: Preparation of vitronectin receptor antagonist
pharmaceuticalsINVENTOR(S): Cheesman, Edward H.; Barrett, John A.; Carpenter, Alan
P., Jr.; Rajopadhye, Milind; Sworin, Michael

PATENT ASSIGNEE(S): Dupont Pharmaceuticals Company, USA

SOURCE: PCT Int. Appl., 318 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001097861	A2	20011227	WO 2001-US20203	20010621
WO 2001097861	A3	20030227		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2412849	AA	20011227	CA 2001-2412849	20010621
EP 1311292	A2	20030521	EP 2001-950446	20010621
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
PRIORITY APPLN. INFO.:			US 2000-213216P	P 20000621
			WO 2001-US20203	W 20010621

OTHER SOURCE(S): MARPAT 136:54027

AB The invention describes compds. (Q)d-Ln-(Ch)d' (Q is a residue having a benzodiazepine-, benzodiazepinedione-, or dibenzotrihydroannulene-type

moiety, $d = 1-10$, $d' = 1-100$, Ln is a linking group, Ch is a metal-bonding unit) for use in the diagnosis and treatment of cancer in combination therapy in a patient. The present invention also provides novel compds. useful for the treatment of rheumatoid arthritis. Thus, (S,S,S)-4-[N-[3-[3,6-diaza-10-[N-(benzimidazol-2-ylmethyl)-N-methylcarbamoyl]-5-(carboxymethyl)-4-oxobicyclo[5.4.0]undeca-1(7),8,10-trien-3-yl]propyl]carbamoyl]-4-[[4-carboxy-2-[2-[1,4,7,10-tetraaza-4,7,10-tris(carboxymethyl)cyclodecyl]acetylaminobutanoyl]amino]butanoic acid was prepared (claimed compound). Syntheses of radiopharmaceuticals, e.g., ^{99m}Tc (VnA) (tricine) (phosphine), where VnA represents the vitronectin receptor antagonist, are also described.

IC ICM A61K051-08

CC 34-3 (Amino Acids, Peptides, and Proteins)

Section cross-reference(s): 8, 28, 63, 78

IT 5704-04-1DP, Tricine, amino acid derivative technetium-99m TPPTS complexes
63995-70-0DP, TPPTS, amino acid derivative technetium-99m tricine complexes
277327-58-9P 277327-59-0P 277327-61-4P 277327-62-5P 277327-64-7P
277327-65-8P 277327-66-9P 277327-67-0P 277327-70-5P 277328-39-9P
277328-40-2P 277328-41-3P 277328-42-4P 277328-43-5P 277328-45-7P
277328-46-8P 277328-47-9P 277328-48-0P 277328-50-4DP,
technetium-99m tricine TPPTS complexes 278180-25-9P 278180-26-0P
278180-27-1P 278180-28-2P 278180-29-3P 278180-30-6P 278180-31-7P
278180-32-8P 278180-36-2P 278180-38-4P 278180-40-8DP,
indium-111-labeled

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)

(preparation of vitronectin receptor antagonist pharmaceuticals)

IT 50-07-7, Mitomycin 57-22-7, Vincristine 57-83-0, Progesterone,
biological studies 59-05-2, Methotrexate 125-84-8, Aminoglutethimide
147-94-4, Cytarabine 302-79-4, Tretinoin 434-07-1, Oxymetholone
488-41-5, Mitobronitol 566-48-3, Formestane 2363-58-8, Epiteostanol
3094-09-5, Doxifluridine 3778-73-2, Ifosfamide 4291-63-8, Cladribine
4533-39-5, Nitracrine 4759-48-2, Isotretinoin 6620-60-6, Proglumide
7723-14-0, Phosphorus-31, biological studies 9014-02-2, Zinostatin
9050-67-3, Sizofilan 10318-26-0, Mitolactol 10540-29-1, Tamoxifen
13311-84-7, Flutamide 13425-98-4, Improsulfan 14133-76-7D,
Technetium-99, amino acid derivative complexes, biological studies
14158-31-7, Iodine-125, biological studies 14769-73-4, Levamisole
17902-23-7, Tegafur 18016-80-3, Lisuride 18883-66-4, Streptozocin
20830-81-3, Daunorubicin 21362-69-6, Mepitiostane 21416-67-1, Razoxane
22181-94-8, Butocin 22668-01-5 23214-92-8, **Doxorubicin**
24279-91-2, Carboquone 27314-97-2, 3-Amino-1,2,4-benzotriazine-1,4-
dioxide 29069-24-7, Prednimustine 29767-20-2, Teniposide 33419-42-0,
Etoposide 39325-01-4, Picibanil 41575-94-4, Carboplatin 42471-28-3,
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Pentostatin 54350-48-0, Etrexinate 55726-47-1, Enocitabine
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81840-15-5, Vesnarinone 83869-56-1, Colony stimulating factor-2
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95058-81-4, Gemcitabine 95734-82-0, Nedaplatin 98631-95-9, Sobuzoxane
102676-47-1, Fadrozole 104958-90-9 108001-60-1 112809-51-5,
Letrozole 112887-68-0, Raltitrexed 120287-85-6, Cetorelix
173146-27-5, Denileukin diftiox 220264-81-3, 10,13-Dimethyl-1,3,4,6-
tetrahydroxyhelianthrone 220264-83-5 381733-54-6 381733-55-7
381733-56-8 381733-57-9 381733-58-0 381733-59-1

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(preparation of vitronectin receptor antagonist pharmaceuticals)

IT 277328-46-8P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of vitronectin receptor antagonist pharmaceuticals)

IT 277328-46-8P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

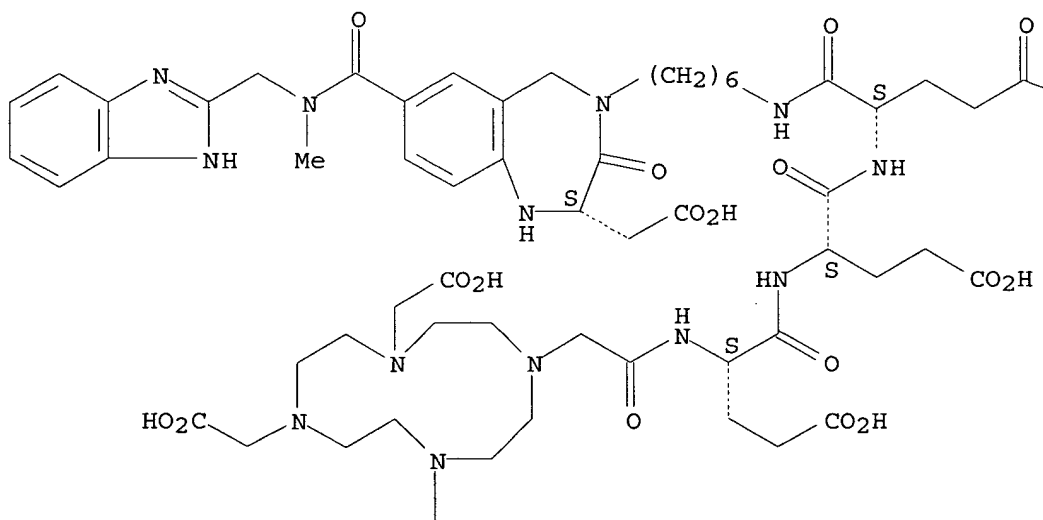
(preparation of vitronectin receptor antagonist pharmaceuticals)

RN 277328-46-8 HCAPLUS

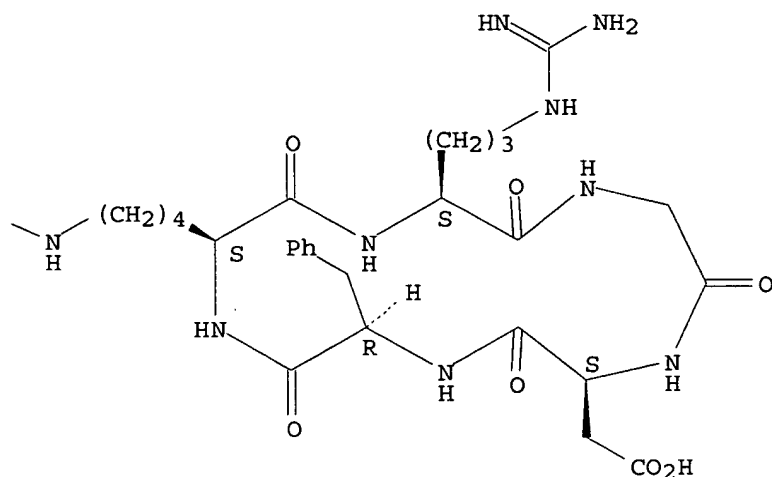
CN Cyclo[L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-N6-[N-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-L- α -glutamyl-L- α -glutamyl-N-[6-[(2S)-7-[[[1H-benzimidazol-2-ylmethyl)methylamino]carbonyl]-2-(carboxymethyl)-1,2,3,5-tetrahydro-3-oxo-4H-1,4-benzodiazepin-4-yl]hexyl]-L- α -glutaminyll-L-lysyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.

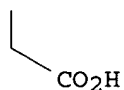
PAGE 1-A



PAGE 1-B



PAGE 2-A



L47 ANSWER 39 OF 43 HCAPLUS COPYRIGHT 2006 ACS on STM
 ACCESSION NUMBER: 2001:935452 HCAPLUS
 DOCUMENT NUMBER: 136:70083
 TITLE: Pharmaceuticals for the imaging of angiogenic disorders for use in combination therapy
 INVENTOR(S): Rajopadhye, Milind; Edwards, D. Scott; Barrett, John A.; Carpenter, Alan P., Jr.; Heminway, Stuart J.; Liu, Shuang; Singh, Prahlad
 PATENT ASSIGNEE(S): Dupont Pharmaceuticals Company, USA
 SOURCE: PCT Int. Appl., 306 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001097860	A2	20011227	WO 2001-US20108	20010621
WO 2001097860	A3	20030227		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
CA 2413328	AA	20011227	CA 2001-2413328	20010621

EP 1311302 A2 20030521 EP 2001-946697 20010621
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 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
 JP 2005538030 T2 20051215 JP 2002-503343 20010621
 PRIORITY APPLN. INFO.: US 2000-213206P P 20000621
 WO 2001-US20108 W 20010621

OTHER SOURCE(S): MARPAT 136:70083

AB Compsds. (Q)d-Ln-Ch (Q is a peptide, d = 1-10, Ln is a linking group, Ch is a metal-bonding unit) were prepared for use in the diagnosis and treatment of cancer in combination therapy in a patient. The present invention also provides novel compds. useful for the treatment of rheumatoid arthritis (no data). Thus, cyclo{Arg-Gly-Asp-D-Tyr(N-[2-[[[5-[carbonyl]-2-pyridinyl]hydrazono]methyl]benzenesulfonic acid]-3-aminopropyl)-Val} was prepared by acylation of cyclo{Arg-Gly-Asp-D-Tyr(3-aminopropyl)-Val} with 2-[[[5-[[2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]-2-pyridinyl]hydrazono]methyl]benzenesulfonic acid monosodium salt and converted into radiopharmaceutical ^{99m}Tc(VnA) (tricine) (phosphine), where VnA represents the vitronectin receptor antagonist.

IC ICM A61K051-08

CC 34-3 (Amino Acids, Peptides, and Proteins)

Section cross-reference(s): 8, 63, 78

IT 50-07-7, Mitomycin 57-22-7, Vincristine 57-83-0, Progesterone,
 biological studies 59-05-2, Methotrexate 125-84-8, Aminogluthethimide
 147-94-4, Cytarabine 302-79-4, Tretinoin 434-07-1, Oxymetholone
 488-41-5, Mitobronitol 566-48-3, Formestane 2363-58-8, Epiteostanol
 3094-09-5, Doxifluridine 3778-73-2, Ifosfamide 4291-63-8, Cladribine
 4533-39-5, Nitracrine 4759-48-2, Isotretinoin 6620-60-6, Proglumide
 9014-02-2, Zinostatin 9034-40-6, Lhrf 9050-67-3, Sizofilan
 10318-26-0, Mitolactol 10540-29-1, Tamoxifen 13311-84-7, Flutamide
 13425-98-4, Improsulfan 14769-73-4, Levamisole 17902-23-7, Tegafur
 18016-80-3, Lisuride 18883-66-4, Streptozocin 20830-81-3, Daunorubicin
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 51264-14-3, Amsacrine 53643-48-4, Vindesine 53910-25-1, Pentostatin
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 Vinorelbine 74050-98-9, Ketanserin 81627-83-0, Colony stimulating
 factor-1 81840-15-5, Vesnarinone 83869-56-1, Colony stimulating
 factor-2 90357-06-5, Bicalutamide 92118-27-9, Fotemustine
 95058-81-4, Gemcitabine 95734-82-0, Nedaplatin 98631-95-9, Sobuzoxane
 102676-47-1, Fadrozole 104958-90-9 108001-60-1 112809-51-5,
 Letrozole 112887-68-0, Raltitrexed 120287-85-6, Cetorelix
 173146-27-5, Denileukin diftitox

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(anticancer agents as adjuvants in the treatment of cancer with peptide
 derivs. and their radioactive metal complexes)

IT 202930-91-4P 250611-72-4P 250611-73-5P 250611-74-6P
 250611-75-7P 250611-76-8P 250611-77-9P 250611-78-0P
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RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic
 preparation); THU (Therapeutic use); BIOL (Biological study); PREP

(Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of peptide derivs. for the imaging of angiogenic disorders and the treatment of cancer in combination therapy)

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 250614-47-2P 250614-48-3P 851024-71-0P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of peptide derivs. for the imaging of angiogenic disorders and the treatment of cancer in combination therapy)

IT 108-30-5, reactions 288-88-0, 1H-1,2,4-Triazole 5437-45-6, Benzyl bromoacetate 5704-04-1, Tricine 23911-26-4, Diethylenetriaminepentaacetic dianhydride 63995-70-0, Tpts 63995-75-5, TPPMS 64018-22-0, TPPDS 122555-91-3 161552-03-0
 180468-25-1 186305-11-3 194920-62-2 250612-83-0D, resin-bound
 250612-84-1D, resin-bound 250612-85-2D, resin-bound 250612-86-3
 250612-87-4 250612-88-5D, resin-bound 250612-89-6D, resin-bound
 250612-90-9D, resin-bound 250612-92-1D, resin-bound 250612-93-2D, resin-bound 250612-94-3

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of peptide derivs. for the imaging of angiogenic disorders and the treatment of cancer in combination therapy)

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 250612-71-6P 250612-72-7P 250612-74-9P 250612-75-0P 250612-77-2P
 250612-78-3P 250612-80-7P 250612-82-9P 250636-75-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of peptide derivs. for the imaging of angiogenic disorders and the treatment of cancer in combination therapy)

IT 202930-91-4P 250611-78-0P 250611-79-1P
 250611-80-4P 250611-81-5P 250611-82-6P
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 250612-06-7P 250612-07-8P 250612-08-9P
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RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of peptide derivs. for the imaging of angiogenic disorders and the treatment of cancer in combination therapy)

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851024-71-0P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of peptide derivs. for the imaging of angiogenic disorders and the treatment of cancer in combination therapy)

IT 161552-03-0

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of peptide derivs. for the imaging of angiogenic disorders and the treatment of cancer in combination therapy)

IT 250612-41-0P 250612-42-1P 250612-43-2P

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250612-50-1P 250612-82-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of peptide derivs. for the imaging of angiogenic disorders and the treatment of cancer in combination therapy)

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250611-83-7P 250611-84-8P 250611-85-9P

250612-06-7P 250612-07-8P 250612-08-9P

250612-09-0P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of peptide derivs. for the imaging of angiogenic disorders and the treatment of cancer in combination therapy)

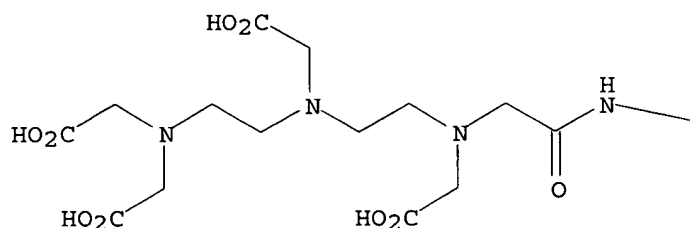
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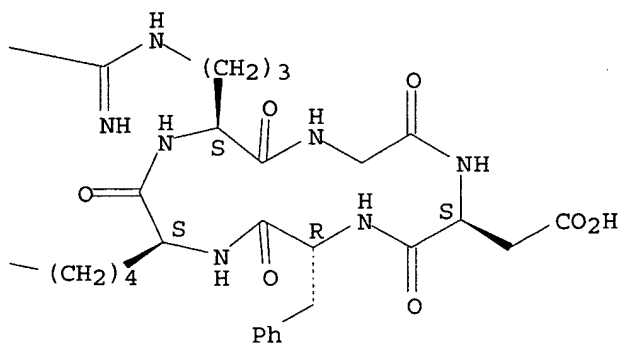
Absolute stereochemistry.

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H₂N—



PAGE 1-B

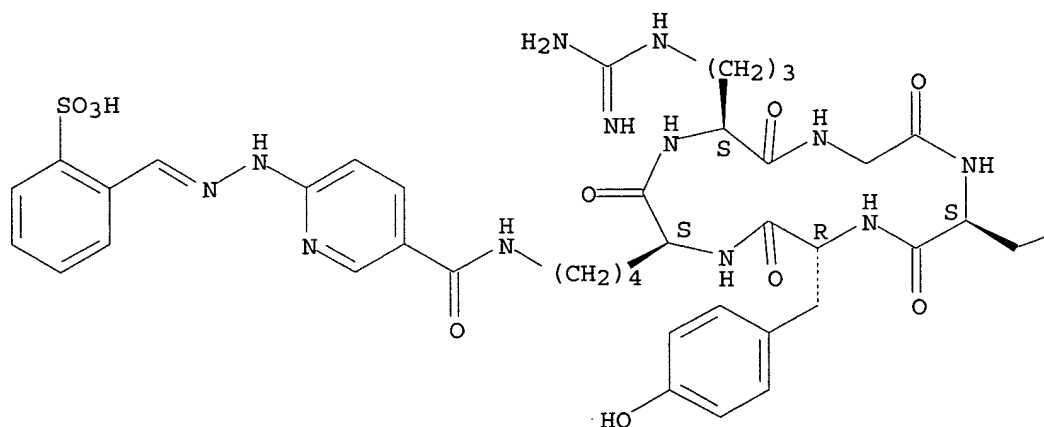


RN 250611-78-0 HCAPLUS

CN Cyclo[L-arginylglycyl-L- α -aspartyl-D-tyrosyl-N6-[[6-[[[2-sulfophenyl)methylene]hydrazino]-3-pyridinyl]carbonyl]-L-lysyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

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PAGE 1-B

—CO₂H

RN 250611-79-1 HCAPLUS

CN Cyclo[L-arginylglycyl-L- α -aspartyl-D-tyrosyl-N6-[[6-[[[2-sulfohenyl)methylene]hydrazino]-3-pyridinyl]carbonyl]-L-lysyl],
mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

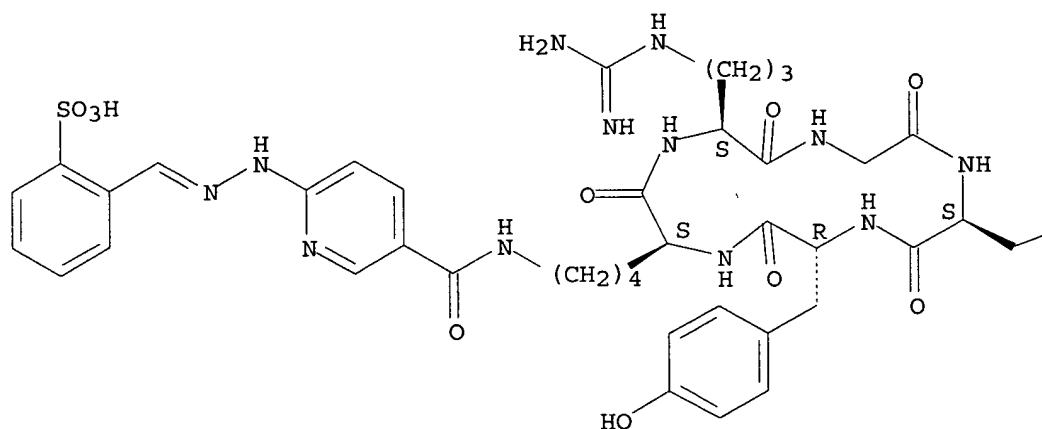
CM 1

CRN 250611-78-0

CMF C40 H50 N12 O12 S

Absolute stereochemistry.
Double bond geometry unknown.

PAGE 1-A



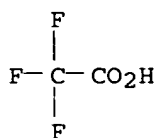
PAGE 1-B

CO₂H

CM 2

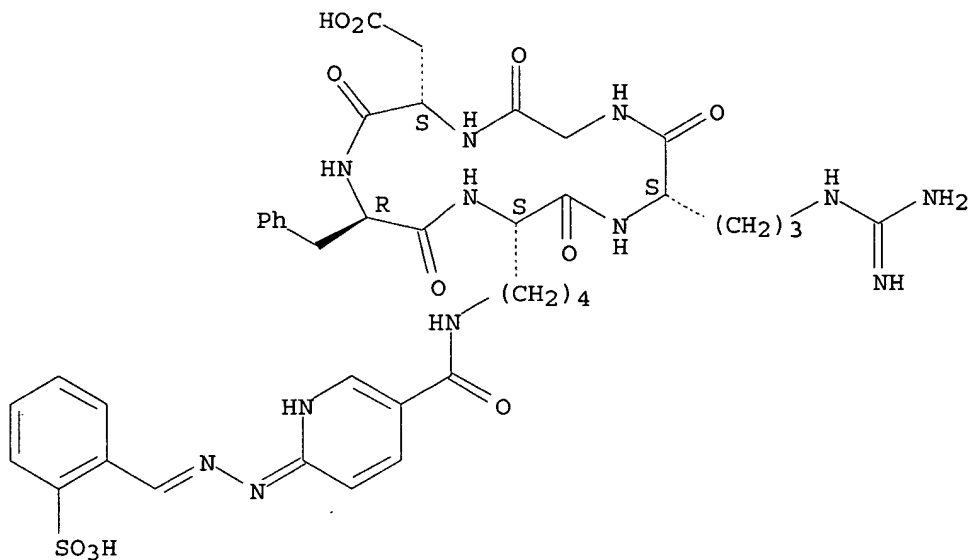
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CMF C2 H F3 O2



RN 250611-80-4 HCAPLUS
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Absolute stereochemistry.
 Double bond geometry unknown.

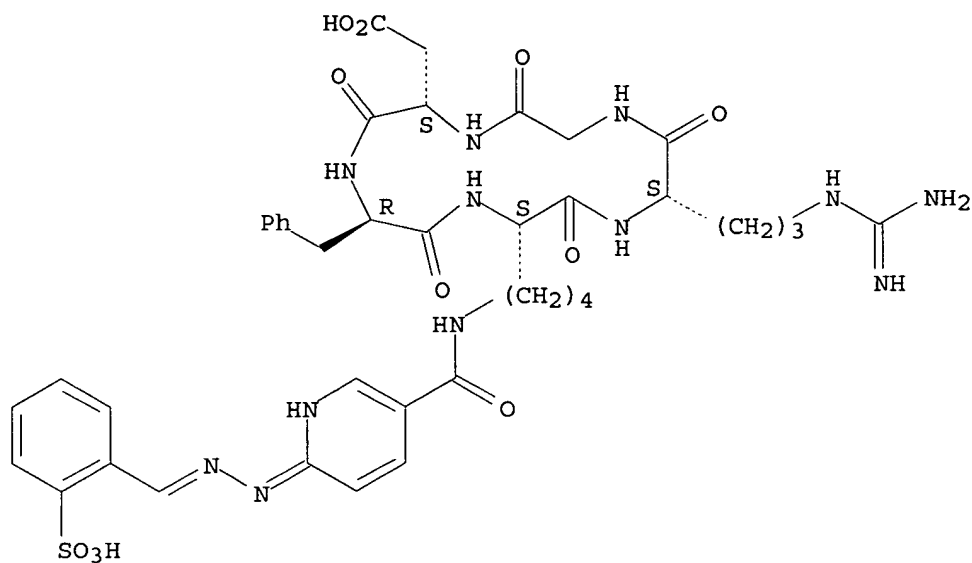


RN 250611-81-5 HCAPLUS
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CM 1

CRN 250611-80-4
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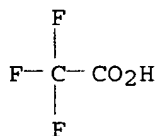
Absolute stereochemistry.
 Double bond geometry unknown.



CM 2

CRN 76-05-1

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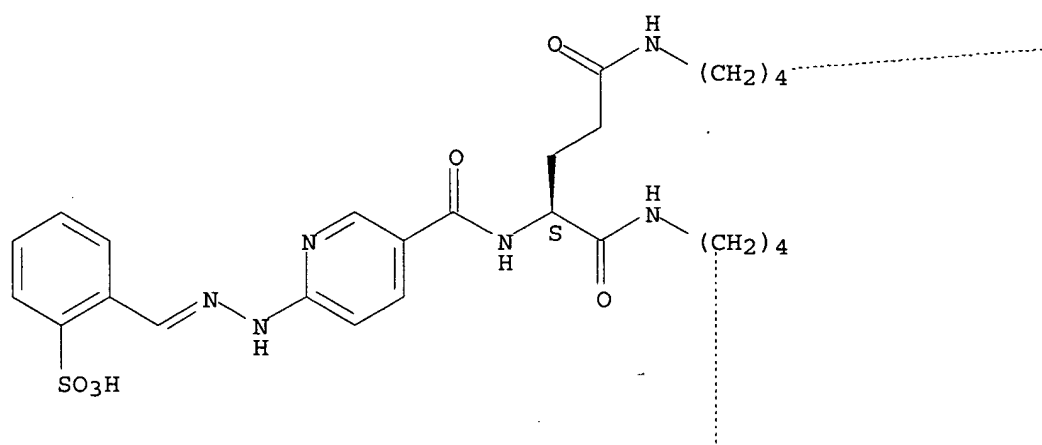
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glutamoyl]bis- (9CI) (CA INDEX NAME)

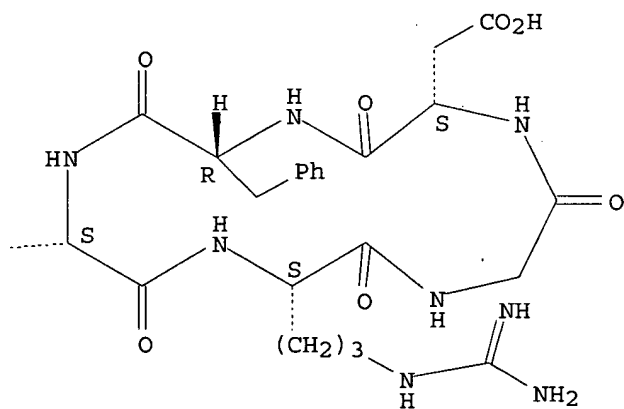
Absolute stereochemistry.

Double bond geometry unknown.

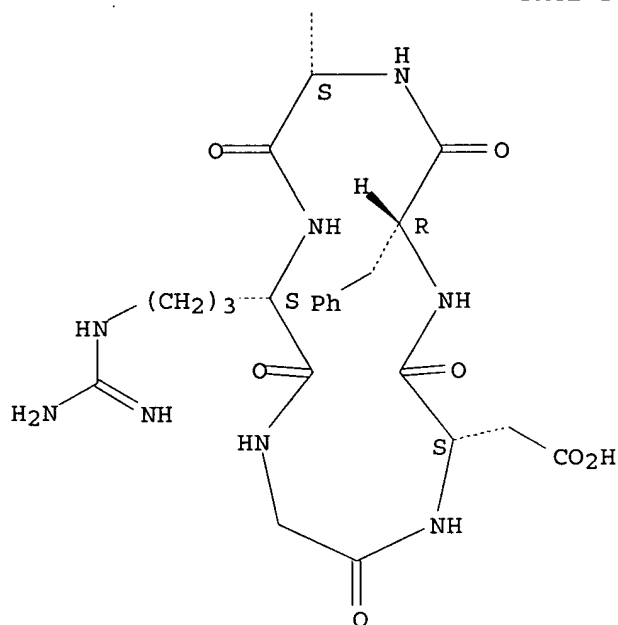
PAGE 1-A



PAGE 1-B



PAGE 2-A



RN 250611-83-7 HCAPLUS

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 glutamoyl]bis-, bis(trifluoroacetate) (9CI) (CA INDEX NAME)

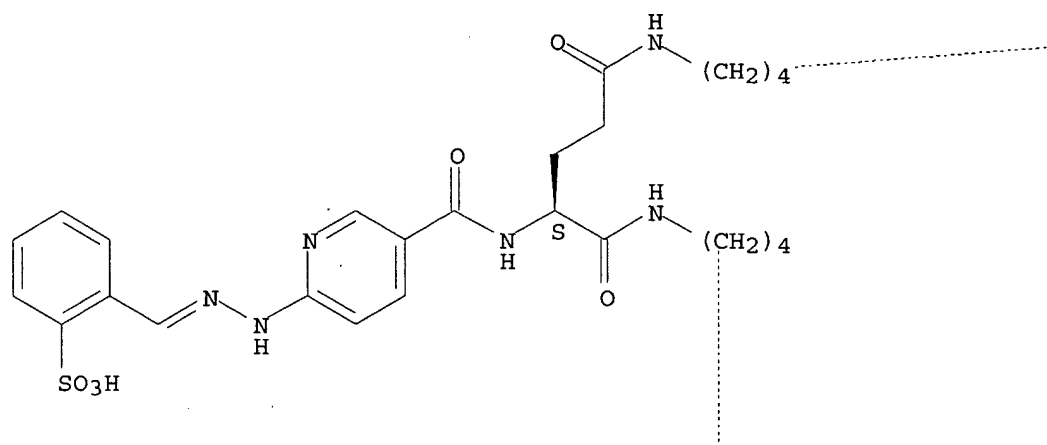
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CRN 250611-82-6

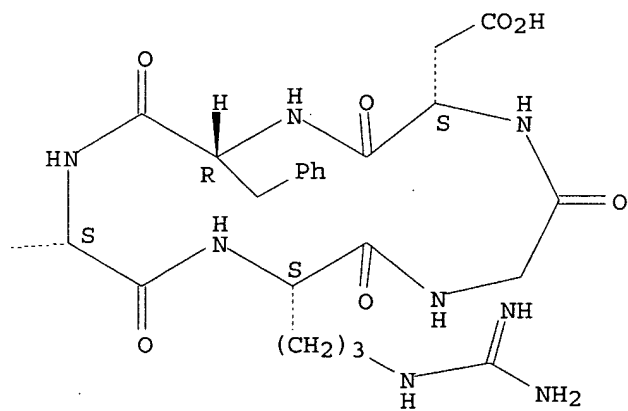
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Absolute stereochemistry.
 Double bond geometry unknown.

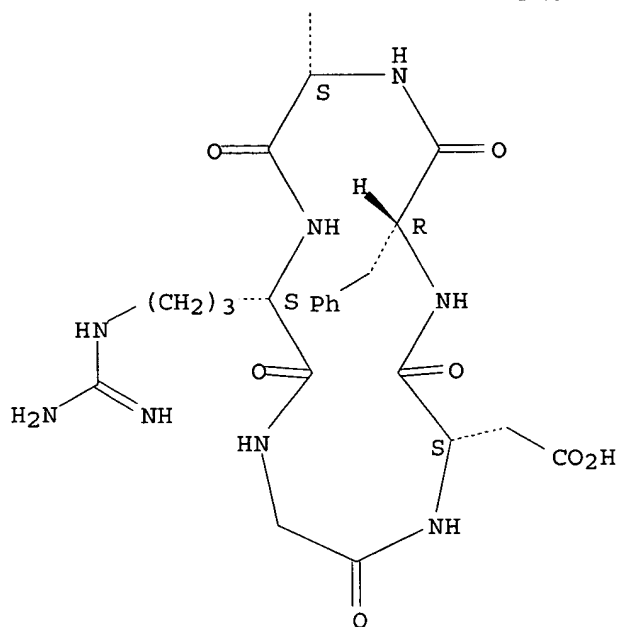
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PAGE 1-B



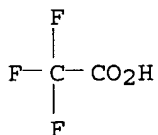
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CM 2

CRN 76-05-1

CMF C2 H F3 O2



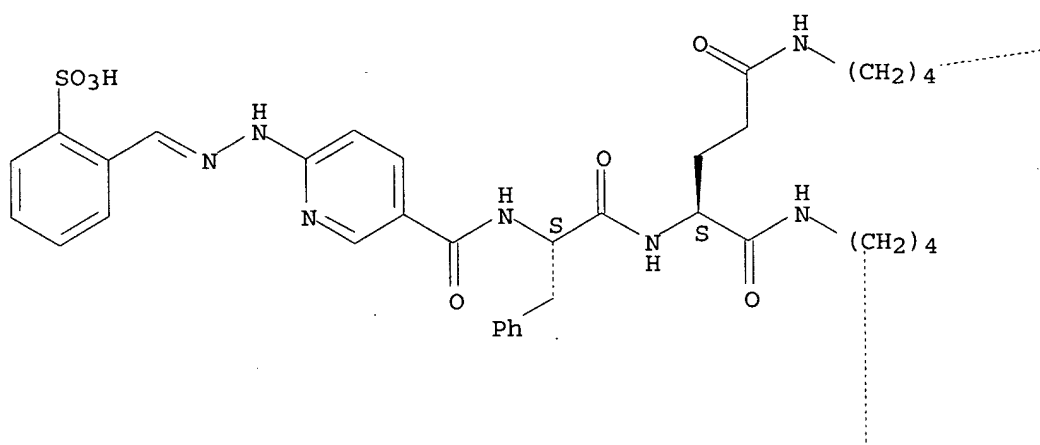
RN 250611-84-8 HCAPLUS

CN Cyclo(L-arginylglycyl-L-α-aspartyl-D-phenylalanyl-L-lysyl),
5,5'-[N-[[6-[[[(2-sulfophenyl)methylene]hydrazino]-3-pyridinyl]carbonyl]-L-
phenylalanyl-L-glutamoyl]bis- (9CI) (CA INDEX NAME)

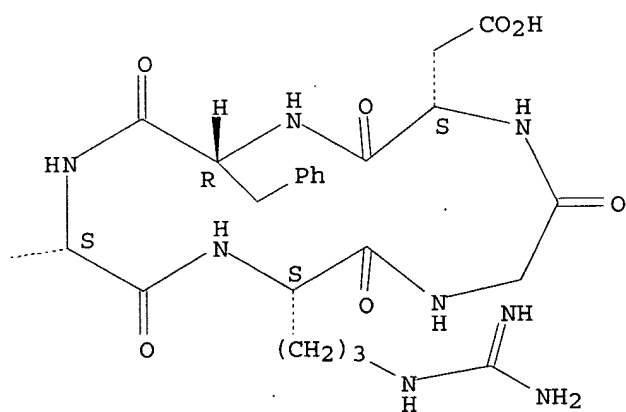
Absolute stereochemistry.

Double bond geometry unknown.

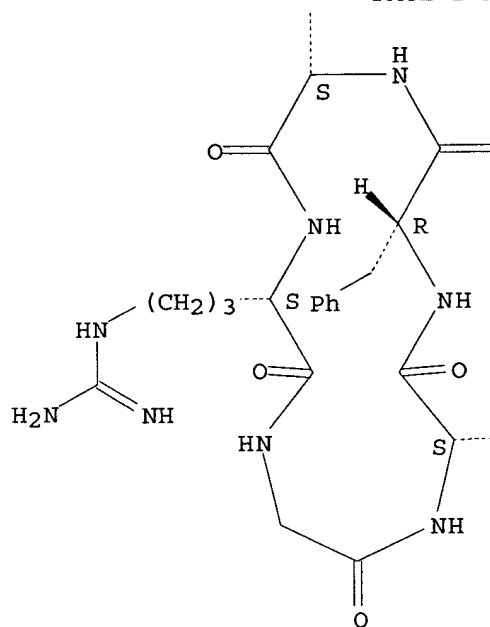
PAGE 1-A



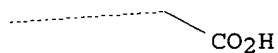
PAGE 1-B



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PAGE 2-B



RN 250611-85-9 HCAPLUS
 CN Cyclo(L-arginylglycyl-L-α-aspartyl-D-phenylalanyl-L-lysyl),
 5,5'-[N-[[6-[[[(2-sulfophenyl)methylene]hydrazino]-3-pyridinyl]carbonyl]-L-
 phenylalanyl-L-glutamoyl]bis-, bis(trifluoroacetate) (9CI) (CA INDEX
 NAME)

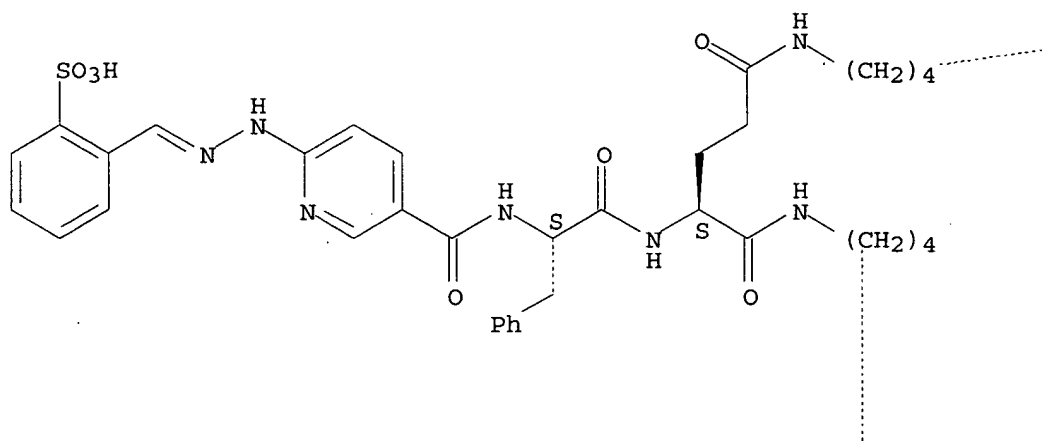
CM 1

CRN 250611-84-8
 CMF C81 H105 N23 O21 S

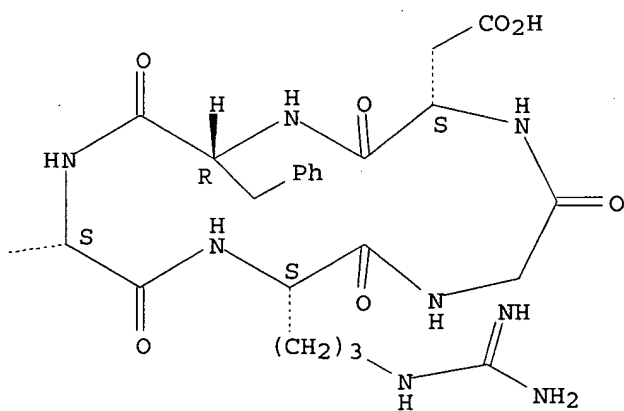
Absolute stereochemistry.

Double bond geometry unknown.

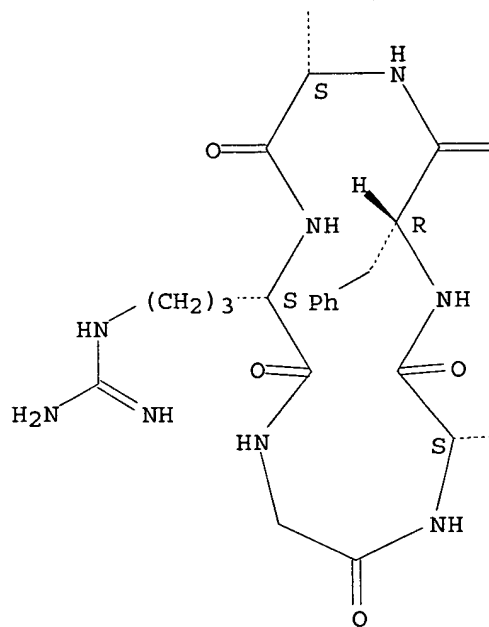
PAGE 1-A



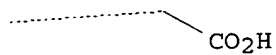
PAGE 1-B



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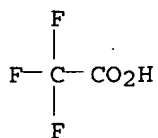
PAGE 2-B



CM 2

CRN 76-05-1

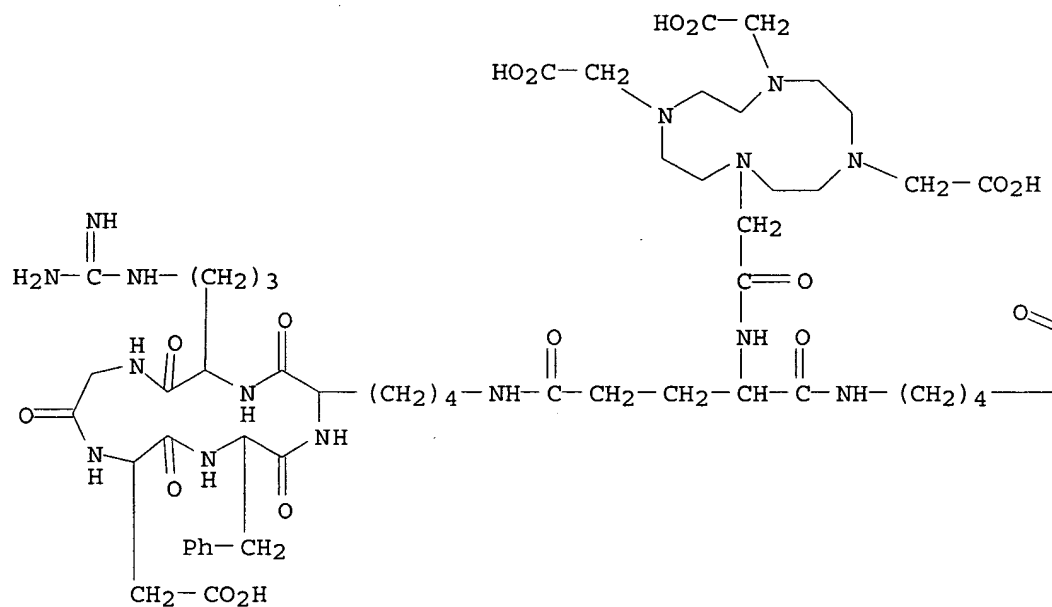
CMF C2 H F3 O2



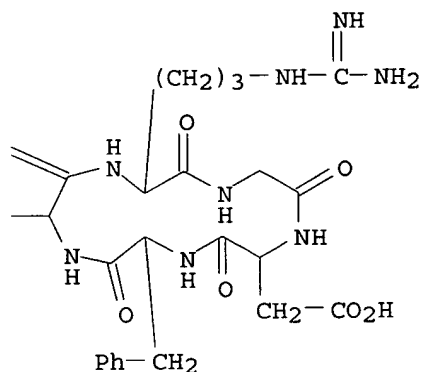
RN 250612-06-7 HCAPLUS

CN Cyclo(L-arginylglycyl-L-α-aspartyl-D-phenylalanyl-L-lysyl),
5,5'-[N-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-L-glutamoyl]bis- (9CI) (CA INDEX NAME)

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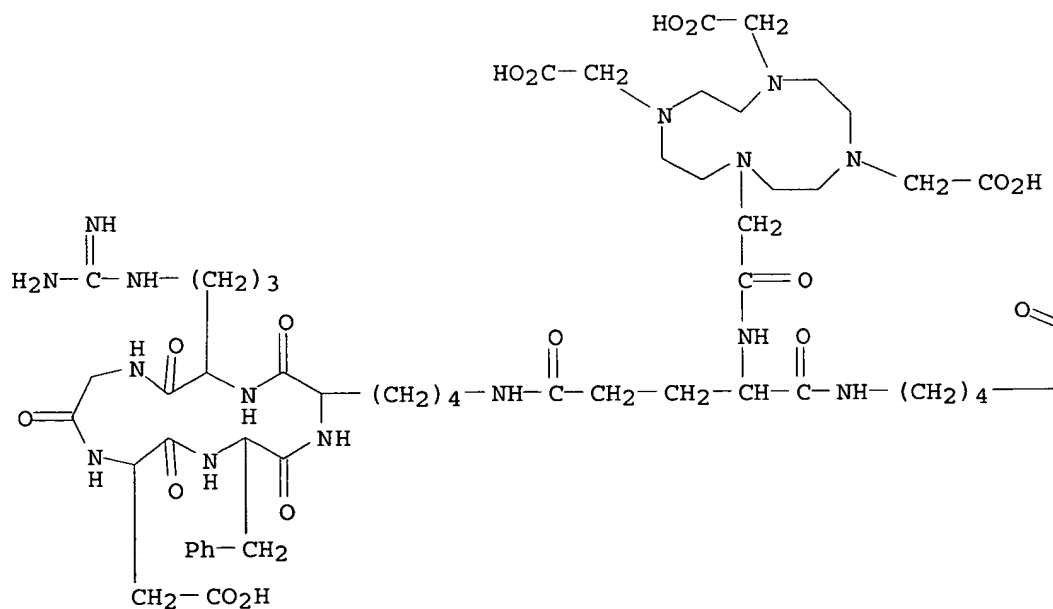
RN 250612-07-8 HCAPLUS
 CN Cyclo(L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-L-lysyl),
 5,5'-[N-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-
 yl]acetyl]-L-glutamoyl]bis-, bis(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

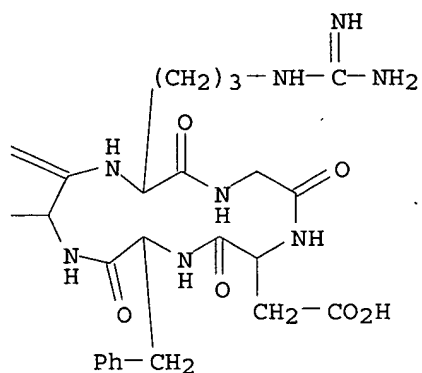
CRN 250612-06-7

CMF C75 H113 N23 O23

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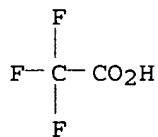
PAGE 1-B



CM 2

CRN 76-05-1

CMF C2 H F3 O2



RN 250612-08-9 HCAPLUS

CN Cyclo[L-arginylglycyl-L-α-aspartyl-D-phenylalanyl-N6-[N-[2-[[2-[bis(carboxymethyl)amino]ethyl](carboxymethyl)amino]ethyl]-N-(carboxymethyl)glycyl]-L-lysyl], mono(trifluoroacetate) (9CI) (CA INDEX NAME)

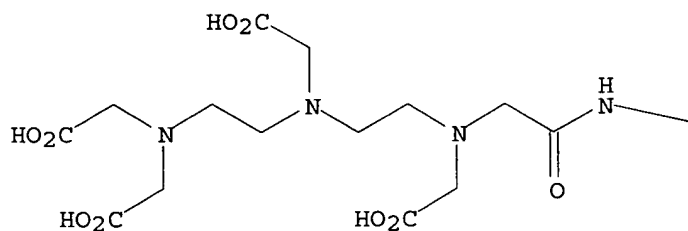
CM 1

CRN 202930-91-4

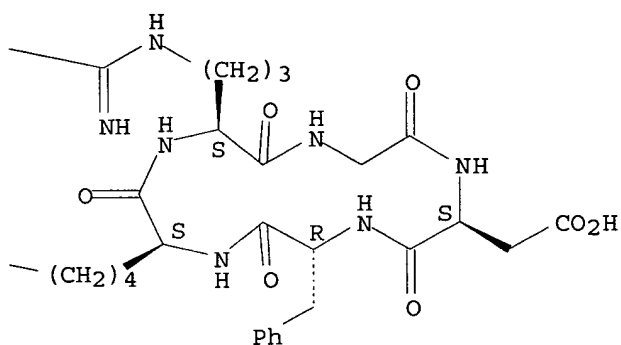
CMF C41 H62 N12 O16

Absolute stereochemistry.

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H₂N—

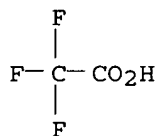
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CM 2

CRN 76-05-1

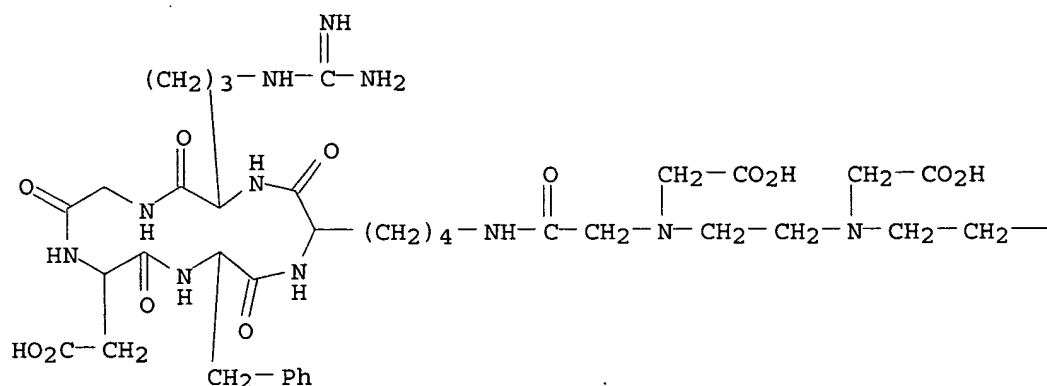
CMF C2 H F3 O2



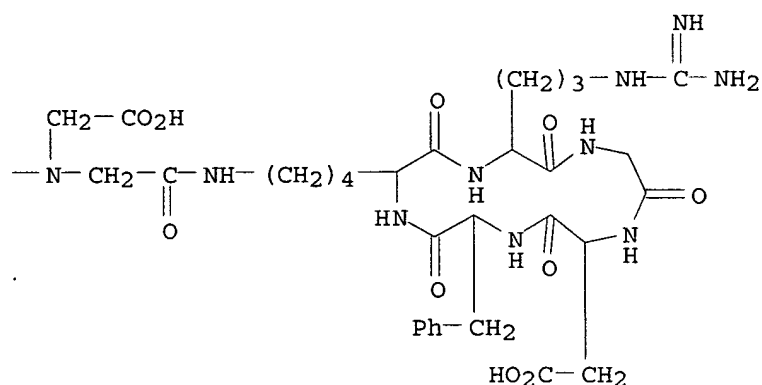
RN 250612-09-0 HCAPLUS

CN Cyclo[L-arginylglycyl-L-α-aspartyl-D-phenylalanyl-N6-[N-(carboxymethyl)glycyl]-L-lysyl], 1',1'''-[[{(carboxymethyl)imino]di-2,1-ethanediyl]bis- (9CI) (CA INDEX NAME)

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IT 250612-24-9P 250612-25-0P 250612-26-1P
 250614-22-3P 250614-23-4P 250614-24-5P
 250614-25-6P 250614-38-1P 250614-39-2P
 250614-41-6P 250614-42-7P 250614-43-8P
 250614-44-9P 250614-46-1P 250614-47-2P
 851024-71-0P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
 (Uses)

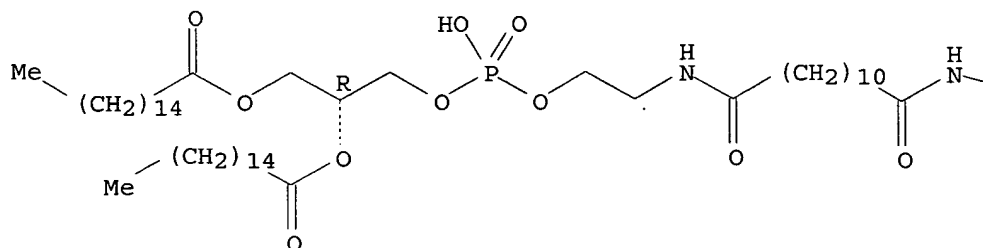
(preparation of peptide derivs. for the imaging of angiogenic disorders and
 the treatment of cancer in combination therapy)

RN 250612-24-9 HCAPLUS

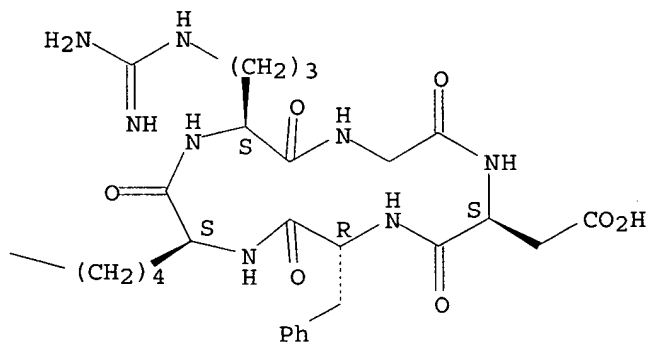
CN Cyclo[L-arginylglycyl-L-α-aspartyl-D-phenylalanyl-N6-[(20R)-17-
 hydroxy-17-oxido-1,12,23-trioxo-20-[(1-oxohexadecyl)oxy]-16,18,22-trioxa-
 13-aza-17-phosphaoctatriacont-1-yl]-L-lysyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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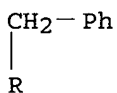
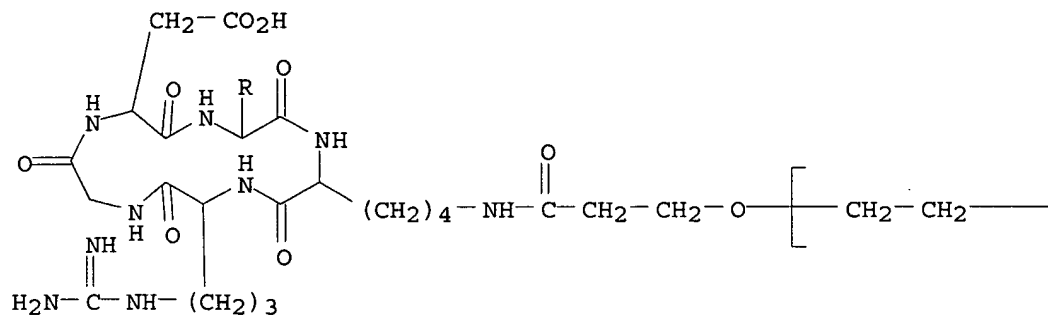


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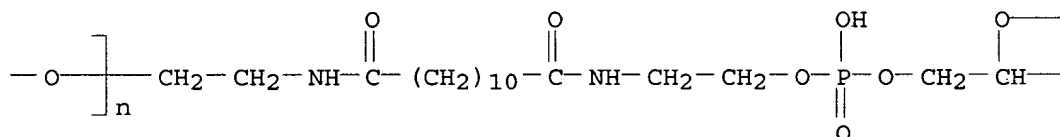


RN 250612-25-0 HCAPLUS
 CN Cyclo[L-arginylglycyl-L-α-aspartyl-D-phenylalanyl-N6-(3-hydroxy-1-oxopropyl)-L-lysyl], ether with α-[(23R)-20-hydroxy-20-oxido-4,15,26-trioxo-23-[(1-oxohexadecyl)oxy]-19,21,25-trioxa-3,16-diaza-20-phosphahentriacont-1-yl]-ω-hydroxypoly(oxy-1,2-ethanediyl) (9CI)
 (CA INDEX NAME)

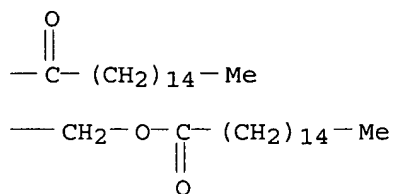
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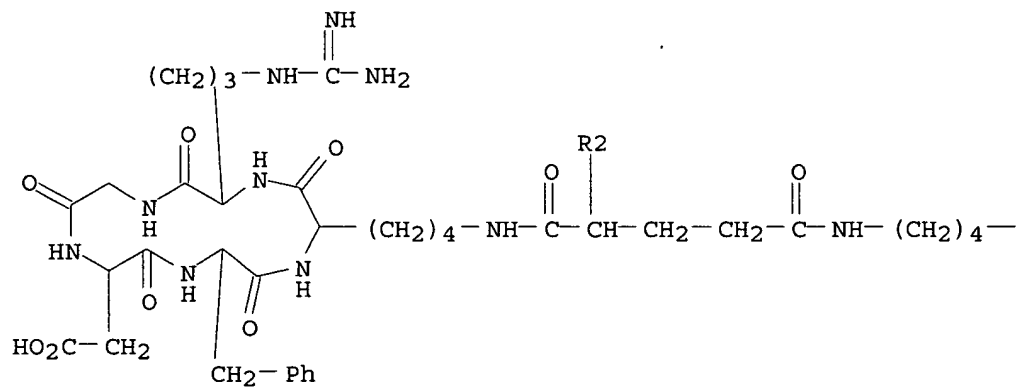
PAGE 1-C



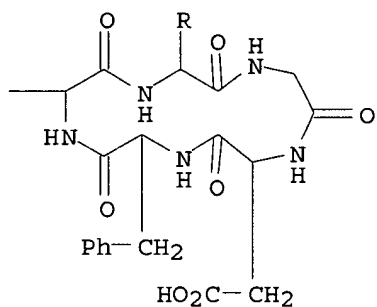
RN 250612-26-1 HCAPLUS

CN Cyclo(L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-L-lysyl),
5,5'-[N-(3-hydroxy-1-oxopropyl)-L-glutamoyl]bis-, ether with
 α -[(23R)-20-hydroxy-20-oxido-4,15,26-trioxo-23-[(1-oxohexadecyl)oxy]-
19,21,25-trioxa-3,16-diaza-20-phosphahentriacont-1-yl]- ω -
hydroxypoly(oxy-1,2-ethanediyl) (9CI) (CA INDEX NAME)

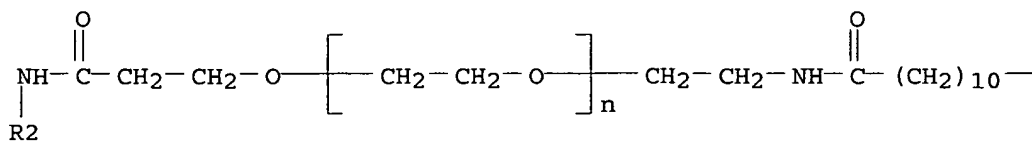
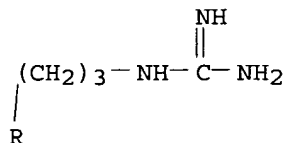
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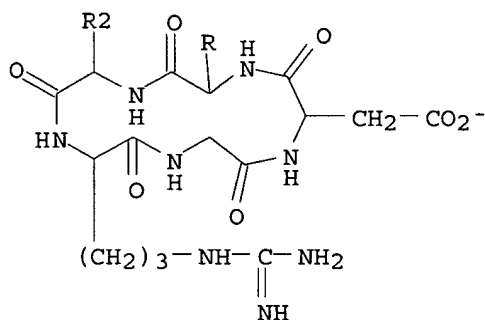
PAGE 2-A



$$\begin{array}{c} \text{O} \\ \parallel \\ -\text{C}-\text{NH}-\text{CH}_2-\text{CH}_2-\text{O}-\text{P}-\text{O}-\text{CH}_2-\text{CH}-\text{CH}_2-\text{O}-\text{C}-\text{(CH}_2\text{)}_{14}\text{-Me} \\ \parallel \qquad \qquad \qquad \parallel \qquad \qquad \qquad \parallel \\ \text{O} \qquad \qquad \qquad \text{OH} \qquad \qquad \qquad \text{O}-\text{C}-\text{(CH}_2\text{)}_{14}\text{-Me} \end{array}$$

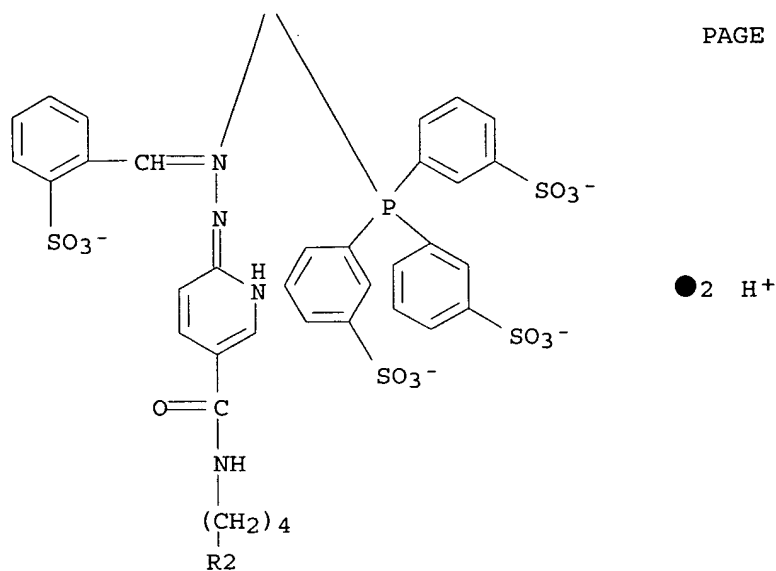
RN	250614-22-3	HCAPLUS
CN	<p>Technetate(5-)-99Tc, [cyclo[L-arginylglycyl-L-α-aspartyl-D-tyrosyl-N6-[[6-[[[2-sulfophenyl)methylene]hydrazino-κN2]-3-pyridinyl]carbonyl]-L-lysylato(2-)]] [N-[2-hydroxy-1,1-bis[(hydroxy-κO)methyl]ethyl]glycinato(3-)-κN,κO] [[3,3',3''-(phosphinidyne-κP)tris[benzenesulfonato]](3-)]-, trisodium dihydrogen (9CI) (CA INDEX NAME)</p>	

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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

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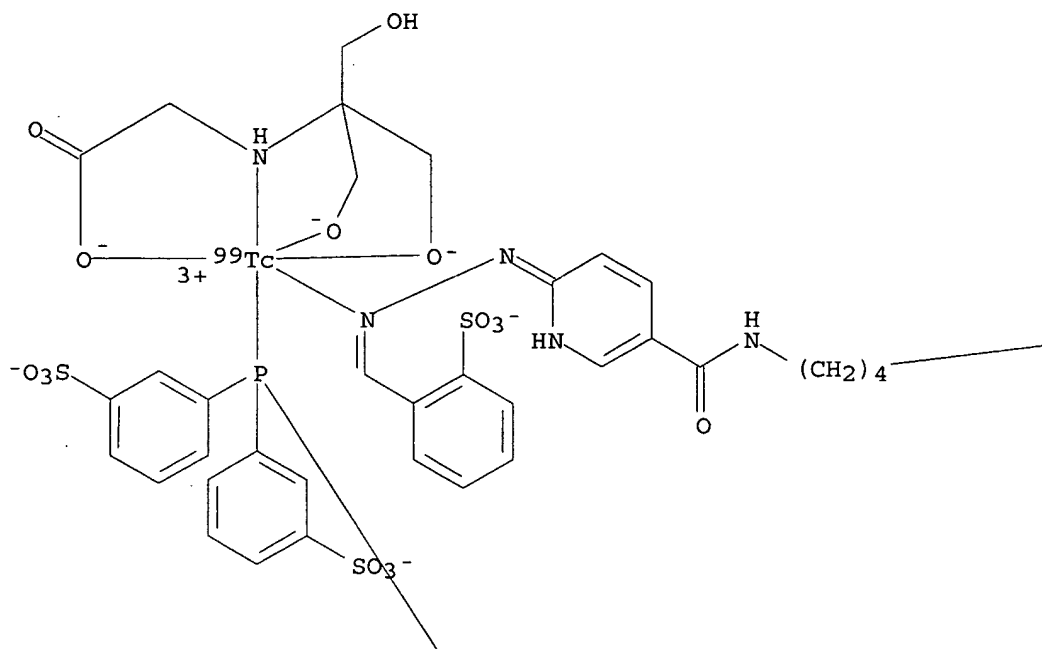


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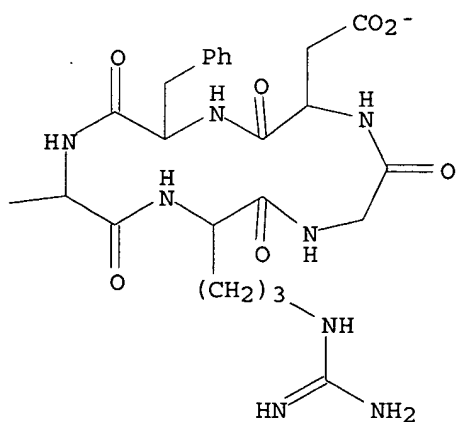
● 3 Na⁺

RN 250614-23-4 HCAPLUS
 CN Technetate(5-) -99Tc, [cyclo[L-arginylglycyl-L-α-aspartyl-D-phenylalanyl-N6-[[6-[[[(2-sulfophenyl)methylene]hydrazino-κN2]-3-pyridinyl]carbonyl]-L-lysylato(2-)]] [N-[2-hydroxy-1,1-bis[(hydroxy-κO)methyl]ethyl]glycinato(3-)-κN,κO] [[3,3',3''-(phosphinidyne-κP)tris[benzenesulfonato]](3-)]-, trisodium dihydrogen (9CI) (CA INDEX NAME)

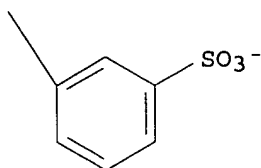
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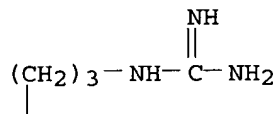
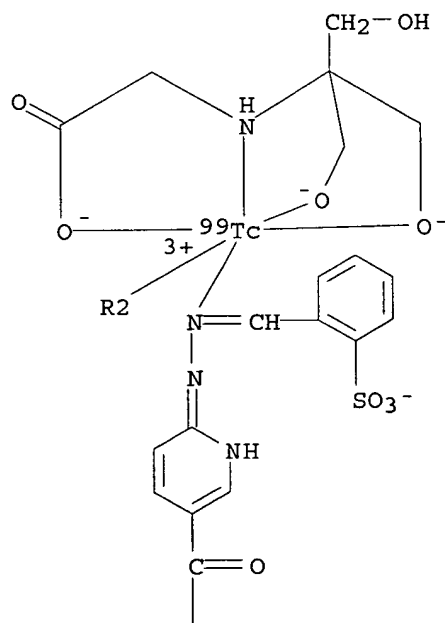


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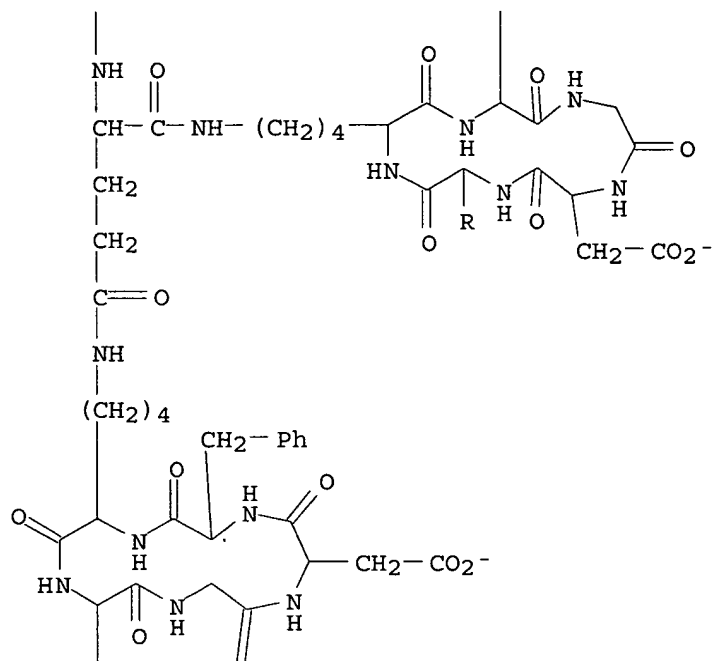
● 2 H⁺● 3 Na⁺

RN 250614-24-5 HCAPLUS
 CN Technetate (6-) -99Tc, [N-[2-hydroxy-1,1-bis[(hydroxy-
 κO)methyl]ethyl]glycinato(3-)-κN,κO] [[3,3',3''-
 (phosphinidyne-κP)tris[benzenesulfonato]](3-)] [[5,5'-[N-[[6-[[[(2-
 sulfophenyl)methylene]hydrazino-κN2]-3-pyridinyl]carbonyl]-L-
 glutamoyl]bis[cyclo(L-arginylglycyl-L-α-aspartyl-D-phenylalanyl-L-
 lysylato)]](3-)]-, trisodium trihydrogen (9CI) (CA INDEX NAME)

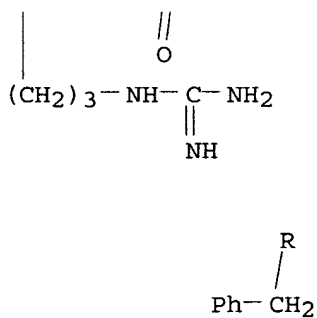
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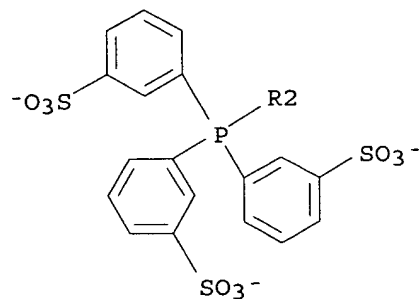
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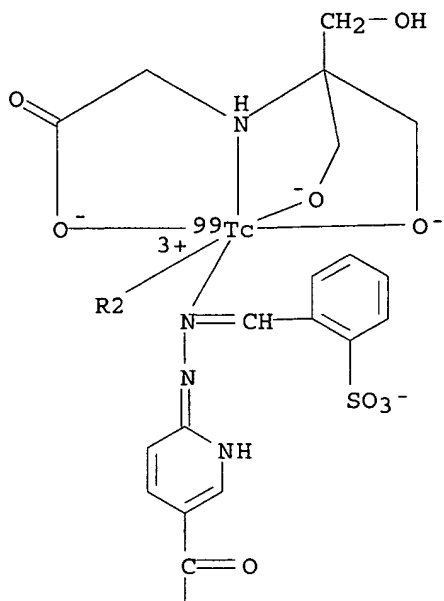


● 3 H⁺

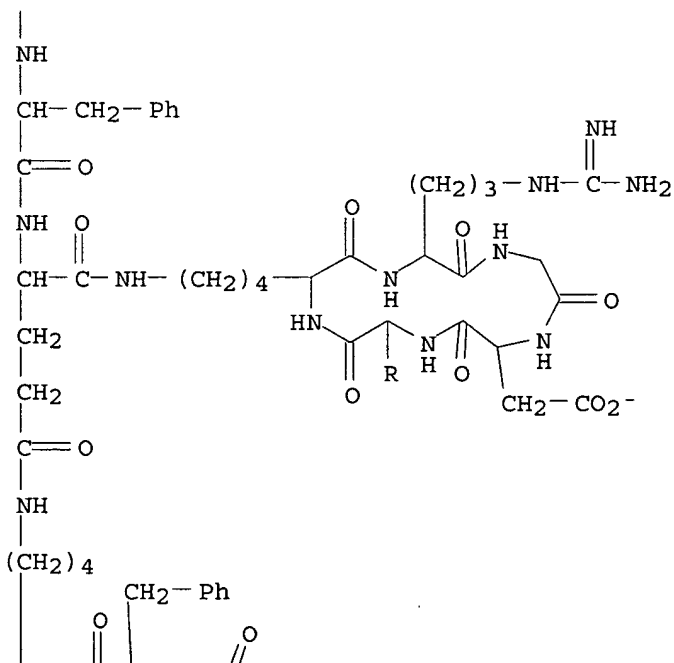
● 3 Na⁺

RN 250614-25-6 HCAPLUS
 CN Technetate(6-)-99Tc, [N-[2-hydroxy-1,1-bis[(hydroxy-
 κO)methyl]ethyl]glycinato(3-)-κN,κO][[3,3',3''-
 (phosphinidyne-κP)tris[benzenesulfonato]](3-)][[5,5'-[N-[[6-[[2-
 sulfophenyl)methylene]hydrazino-κN2]-3-pyridinyl]carbonyl]-L-
 phenylalanyl-L-glutamoyl]bis[cyclo(L-arginylglycyl-L-α-aspartyl-D-
 phenylalanyl-L-lysylato)]](3-)]-, trisodium trihydrogen (9CI) (CA INDEX
 NAME)

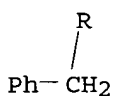
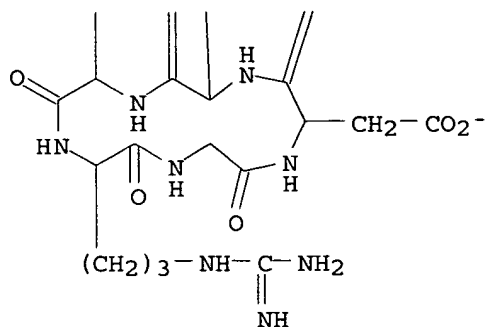
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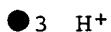
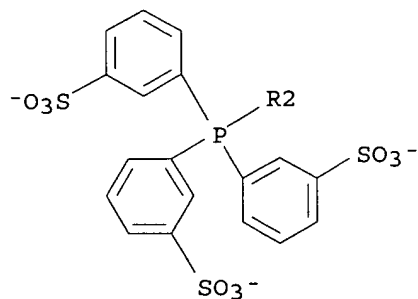
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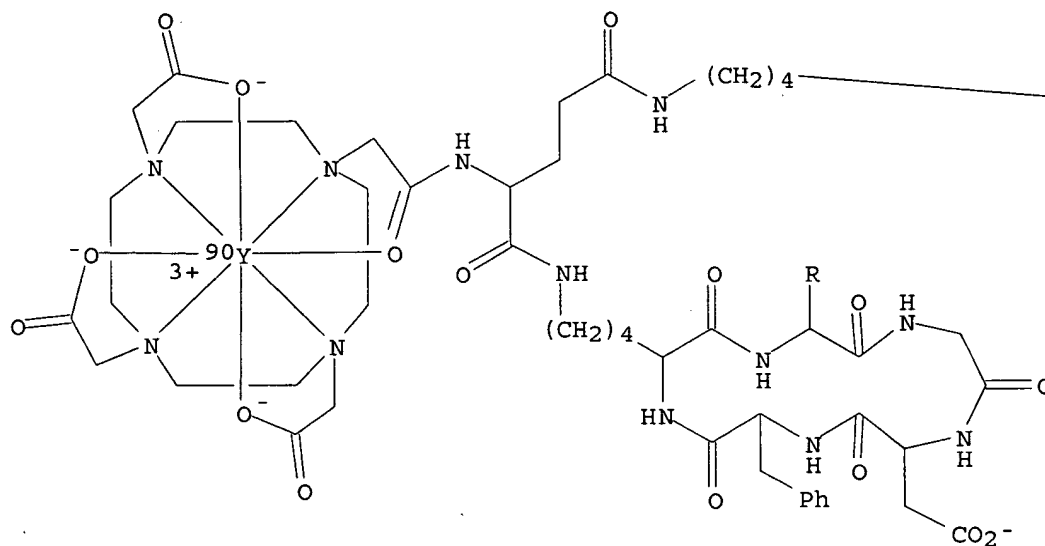


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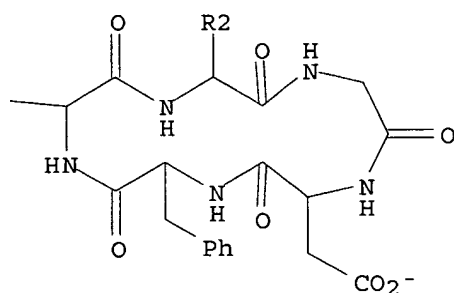


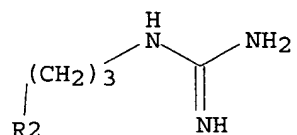
RN 250614-38-1 HCAPLUS
 CN Yttrate(2-)-90Y, [[5,5'-[N-[[4,7,10-tris[(carboxy-κO)methyl]-1,4,7,10-tetraazacyclododec-1-yl-κN1,κN4,κN7,κN10]acetyl-κO]-L-glutamoyl]bis[cyclo(L-arginylglycyl-L-α-aspartyl-D-phenylalanyl-L-lysylato)]](5-)]-, dihydrogen (9CI) (CA INDEX NAME)

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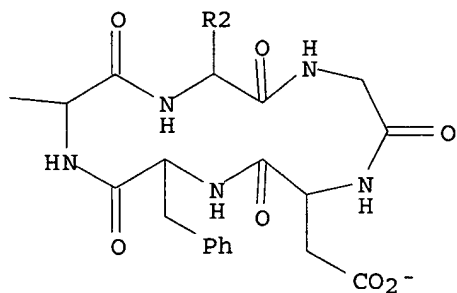


$$\begin{array}{c} \text{H}_2\text{N} \quad \text{NH} \\ \diagdown \quad \diagup \\ \text{C} \\ | \\ \text{HN} - (\text{CH}_2)_3 \\ | \\ \text{R} \end{array}$$


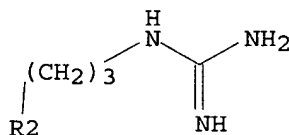
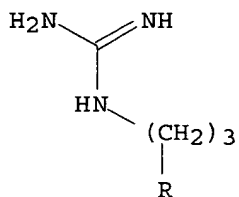
RN	250614-39-2	HCAPLUS
CN	Lutetate(2-)-177Lu, [[5,5'-[N-[[4,7,10-tris[(carboxy-κO)methyl]-1,4,7,10-tetraazacyclododec-1-yl-κN1,κN4,κN7,κN10]acetyl-κO]-L-glutamoyl]bis[cyclo(L-arginylglycyl-L-α-aspartyl-D-phenylalanyl-L-lysylato)]](5-)]-, dihydrogen (9CI) (CA INDEX NAME)	

The diagram shows a $^{177}\text{Lu}^{3+}$ ion coordinated by a macrocyclic ligand. The macrocycle consists of four nitrogen atoms and four oxygen atoms, with a carboxylate group (COO^-) attached to one of the nitrogens. A peptide chain is attached to the macrocycle via an amide bond. The peptide chain includes a phenyl group (Ph), a carboxylate group (COO^-), and a long alkyl chain ($(\text{CH}_2)_4$).

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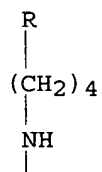
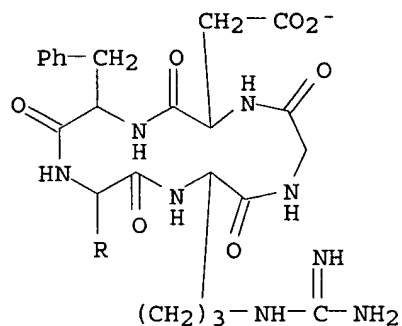
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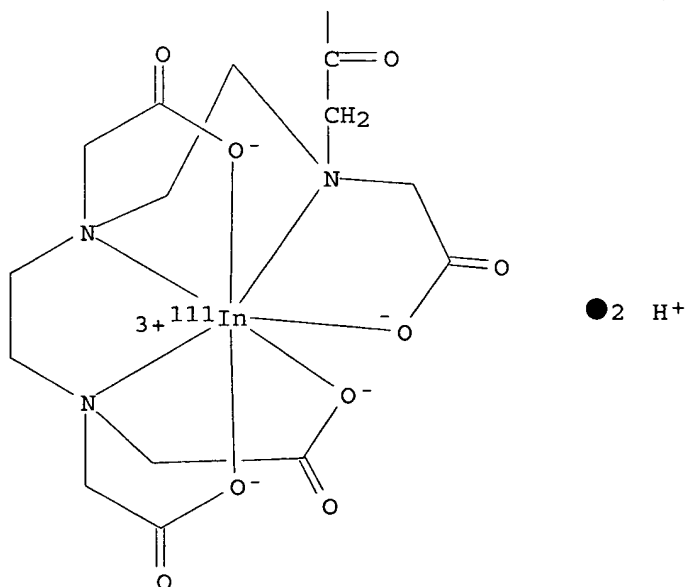
● 2 H⁺

RN 250614-41-6 HCAPLUS
 CN Indate(2-)-111In, [cyclo[L-arginylglycyl-L-α-aspartyl-D-phenylalanyl-N6-[N-[2-[2-[bis[(carboxy-κO)methyl]amino-κN]ethyl][(carboxy-κO)methyl]amino-κN]ethyl]-N-[(carboxy-κO)methyl]glycyl-κN,κO]-L-lysylato(5-)]], dihydrogen (9CI) (CA INDEX NAME)

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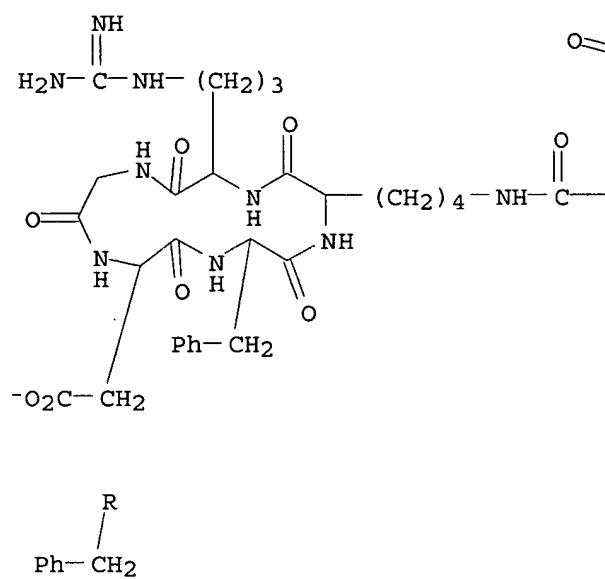


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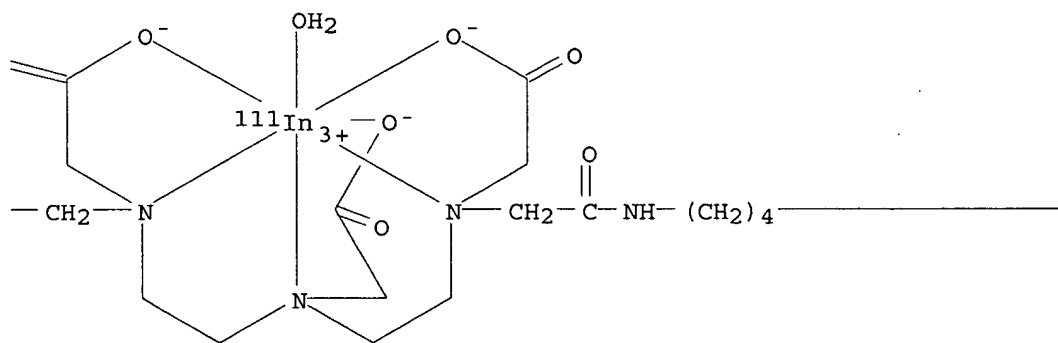


RN 250614-42-7 HCAPLUS
 CN Indate(2-)-111In, aqua[[1',1'''-[[[(carboxy-κO)methyl]imino-κN]di-2,1-ethanediyl]bis[cyclo[L-arginylglycyl-L-α-aspartyl-D-phenylalanyl-N6-[N-[(carboxy-κO)methyl]glycyl-κN]-L-lysylato]]](5-)]-, dihydrogen (9CI) (CA INDEX NAME)

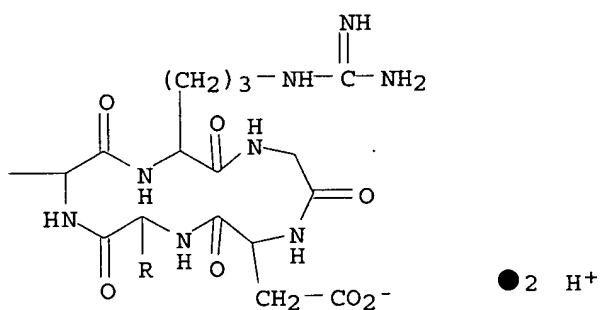
PAGE 1-A



PAGE 1-B

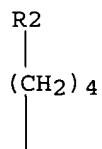
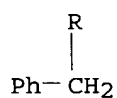
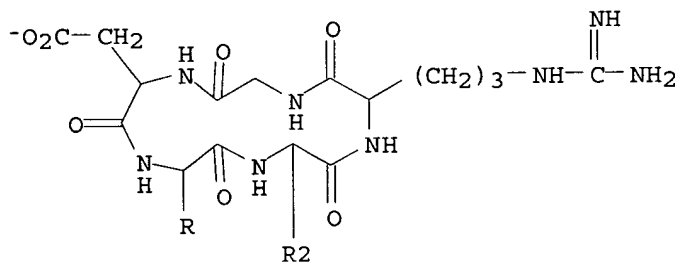


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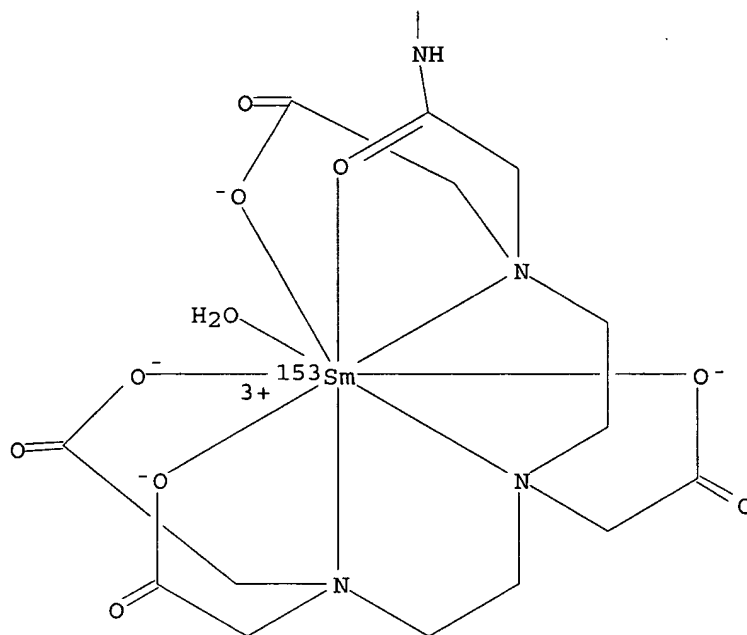


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PAGE 2-A

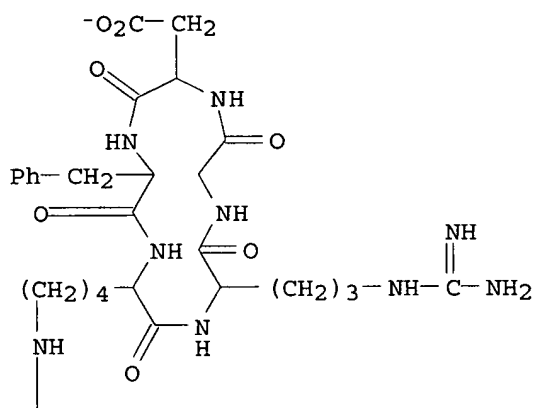


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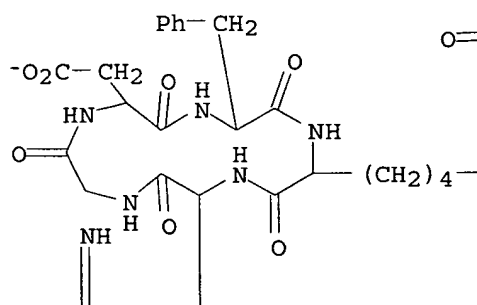
● 2 H⁺

RN 250614-44-9 HCAPLUS
 CN Samarate(2-)-153Sm, [[1',1'''-[[[(carboxy-κO)methyl]imino-κN]di-2,1-ethanediyl]bis[cyclo[L-arginylglycyl-L-α-aspartyl-D-phenylalanyl-N6-[N-[(carboxy-κO)methyl]glycyl-κN]-L-lysylato]]](5-)]-, dihydrogen (9CI) (CA INDEX NAME)

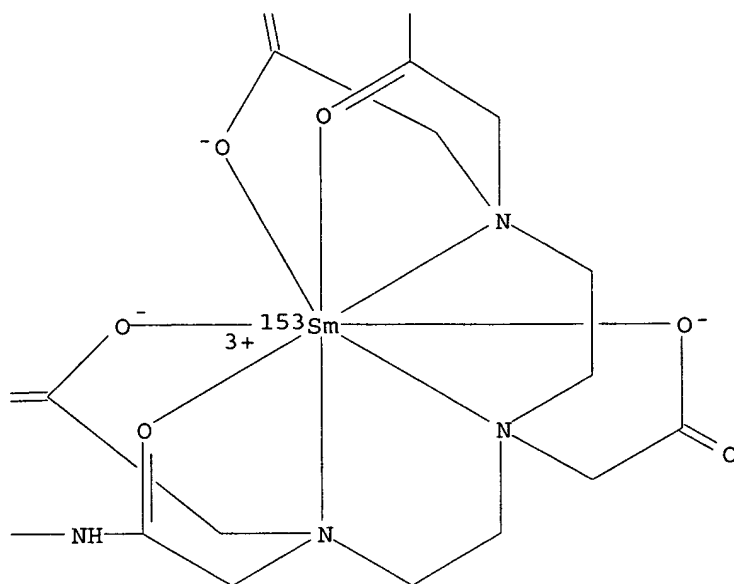
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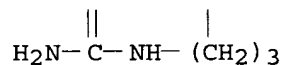
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PAGE 2-B

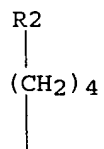
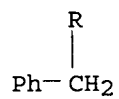
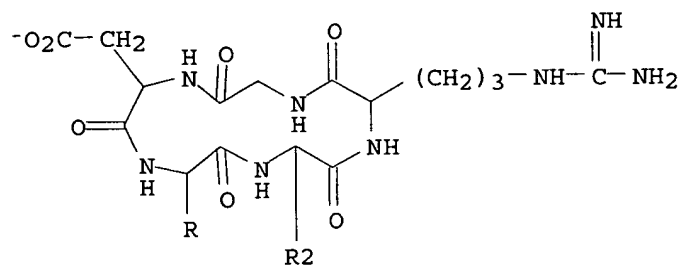


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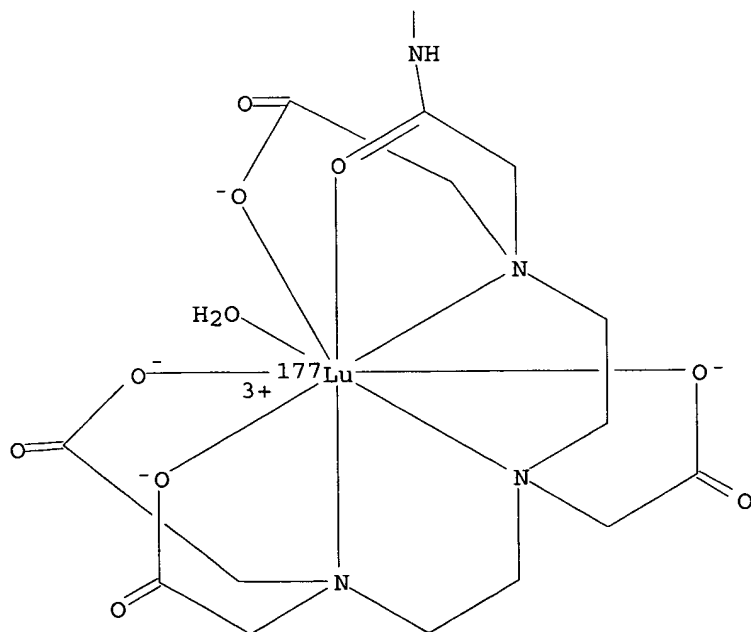
● 2 H⁺

RN 250614-46-1 HCAPLUS
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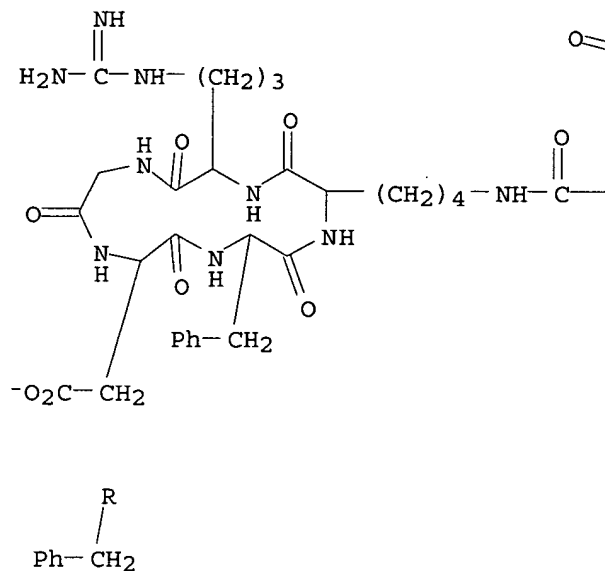
PAGE 3-A

● 2 H⁺

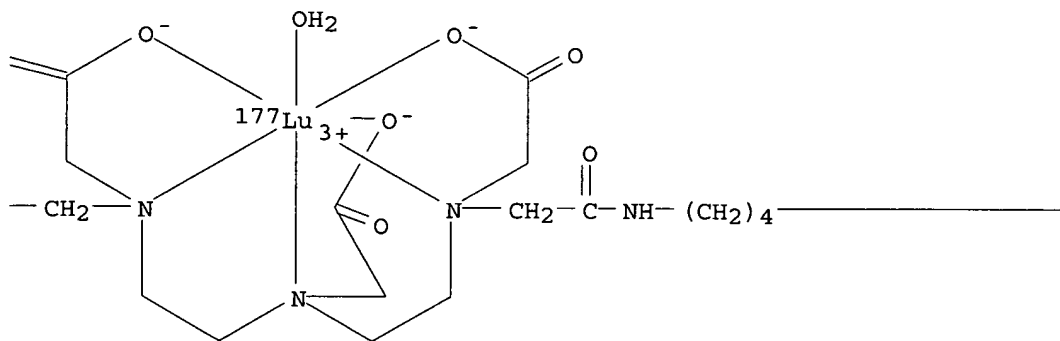
RN 250614-47-2 HCAPLUS

CN Lutetate(2-)-177Lu, aqua[[1',1'''-[[[(carboxy-κO)methyl]imino-κN]di-2,1-ethanediyl]bis[cyclo[L-arginylglycyl-L-α-aspartyl-D-phenylalanyl-N6-[N-[(carboxy-κO)methyl]glycyl-κN]-L-lysylato]]](5-)]-, dihydrogen (9CI) (CA INDEX NAME)

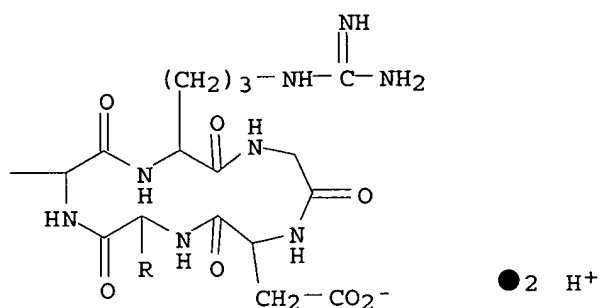
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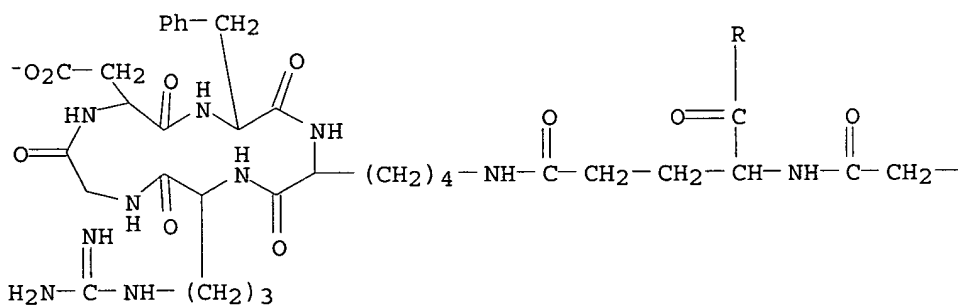


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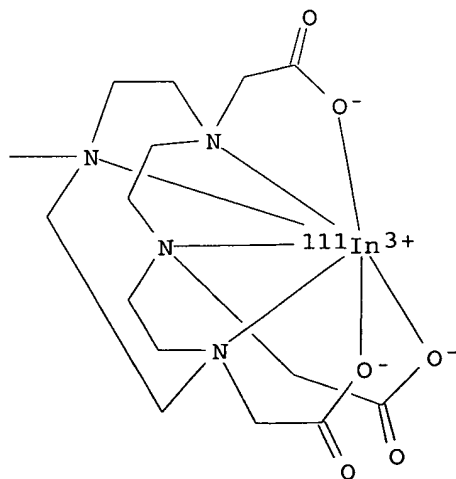


RN 851024-71-0 HCAPLUS
 CN Indate(2-)-111In, [[5,5'-[N-[[4,7,10-tris[(carboxy-κO)methyl]-1,4,7,10-tetraazacyclododec-1-yl-κN1,κN4,κN7,κN10]acetyl]-L-glutamoyl]bis[cyclo[L-arginylglycyl-L-α-aspartyl-D-phenylalanyl-L-lysylato]]](5-)]-, dihydrogen (9CI) (CA INDEX NAME)

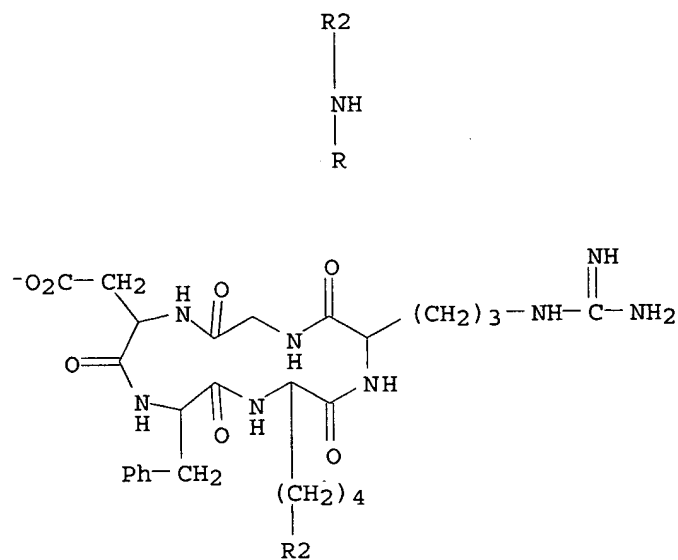
PAGE 1-A



PAGE 1-B



PAGE 2-A



PAGE 2-B

● 2 H⁺

IT 161552-03-0

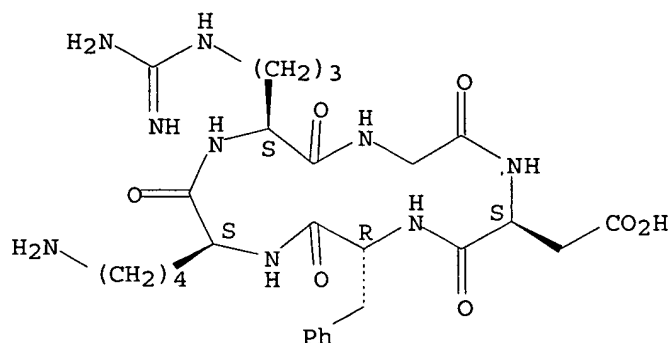
RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of peptide derivs. for the imaging of angiogenic disorders and the treatment of cancer in combination therapy)

RN 161552-03-0 HCAPLUS

CN Cyclo(L-arginylglycyl-L-α-aspartyl-D-phenylalanyl-L-lysyl) (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



IT 250612-41-0P 250612-42-1P 250612-43-2P
250612-44-3P 250612-46-5P 250612-48-7P
250612-50-1P 250612-82-9P

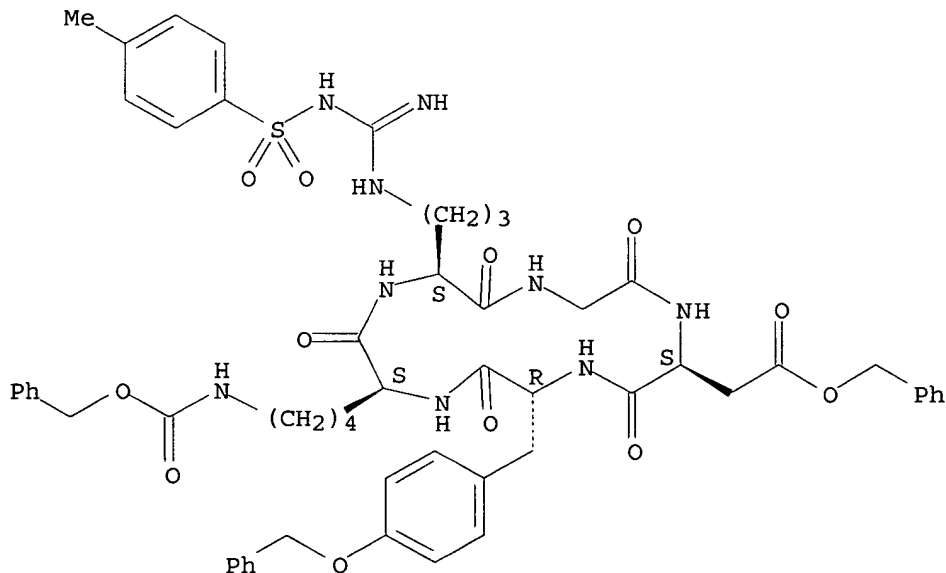
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)

(preparation of peptide derivs. for the imaging of angiogenic disorders and
the treatment of cancer in combination therapy)

RN 250612-41-0 HCAPLUS

CN Cyclo[L- α -aspartyl-O-(phenylmethyl)-D-tyrosyl-N6-
[(phenylmethoxy) carbonyl]-L-lysyl-N5-[imino[[4-
methylphenyl)sulfonyl]amino]methyl]-L-ornithylglycyl], phenylmethyl ester
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 250612-42-1 HCAPLUS

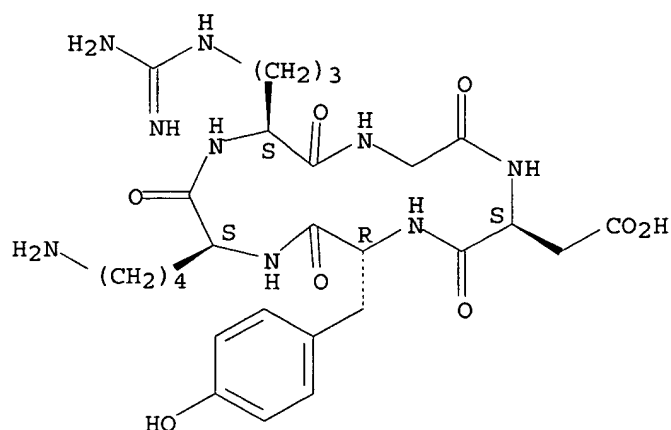
CN Cyclo(L-arginylglycyl-L- α -aspartyl-D-tyrosyl-L-lysyl),
bis(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

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CRN 217099-14-4

CMF C27 H41 N9 O8

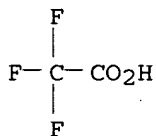
Absolute stereochemistry.



CM 2

CRN 76-05-1

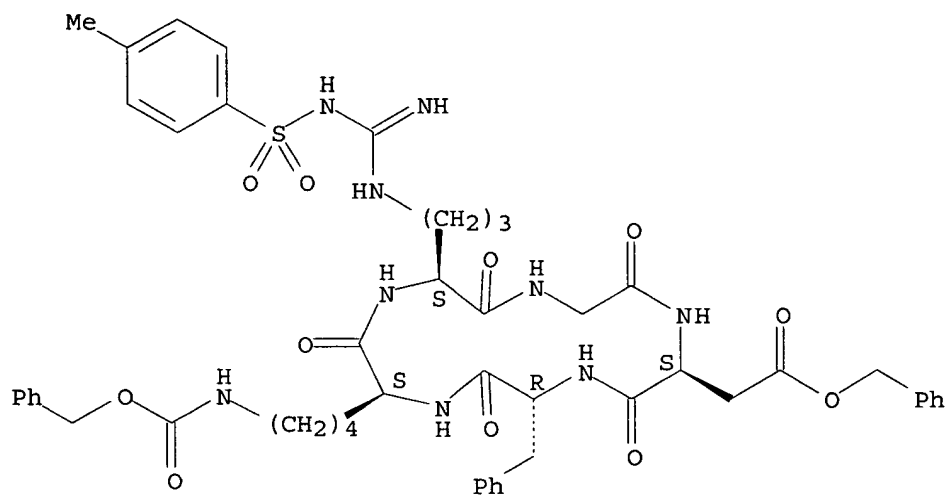
CMF C2 H F3 O2



RN 250612-43-2 HCAPLUS

CN Cyclo[L- α -aspartyl-D-phenylalanyl-N6-[(phenylmethoxy)carbonyl]-L-lysyl-N5-[imino[[4-methylphenyl)sulfonyl]amino]methyl]-L-ornithylglycyl], phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 250612-44-3 HCAPLUS

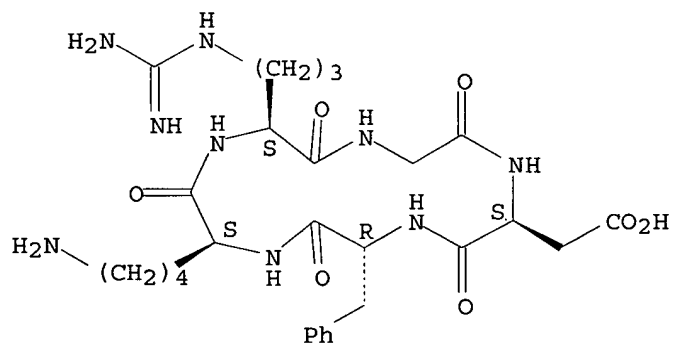
CN Cyclo(L-arginylglycyl-L-α-aspartyl-D-phenylalanyl-L-lysyl),
bis(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 161552-03-0

CMF C27 H41 N9 O7

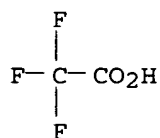
Absolute stereochemistry.



CM 2

CRN 76-05-1

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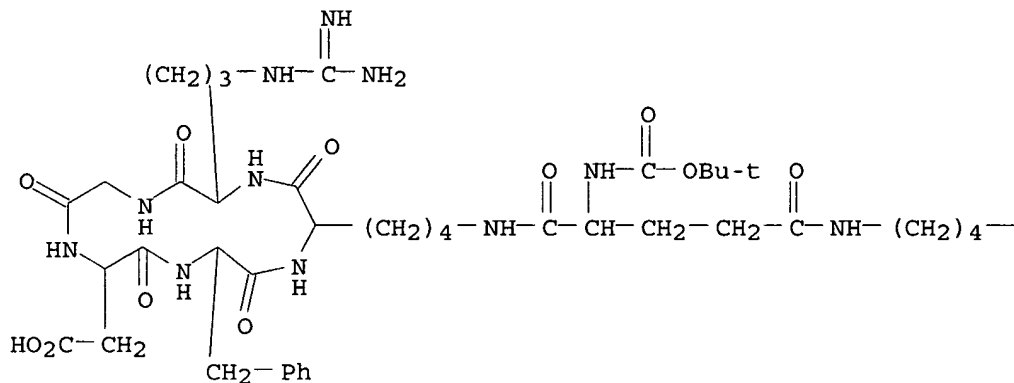


RN 250612-46-5 HCAPLUS
 CN Cyclo(L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-L-lysyl),
 5,5'-[N-[(1,1-dimethylethoxy)carbonyl]-L-glutamoyl]bis-,
 bis(trifluoroacetate) (9CI) (CA INDEX NAME)

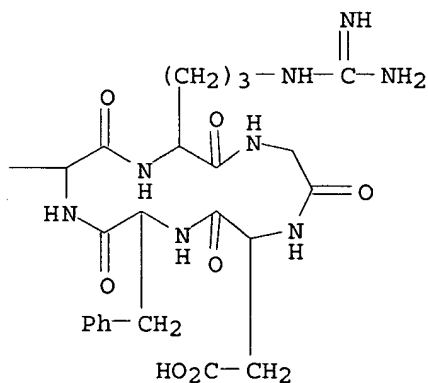
CM 1

CRN 250612-45-4
 CMF C64 H95 N19 O18

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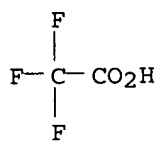


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CM 2

CRN 76-05-1
 CMF C2 H F3 O2

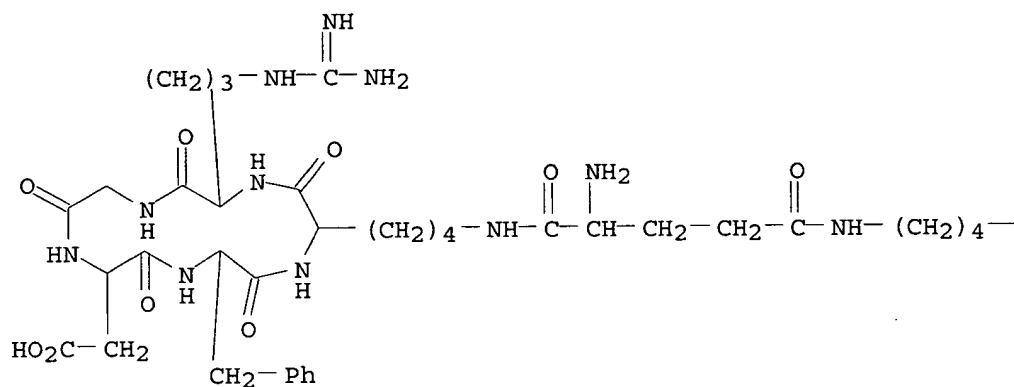


RN 250612-48-7 HCAPLUS
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 5,5'-L-glutamoylbis-, tris(trifluoroacetate) (9CI) (CA INDEX NAME)

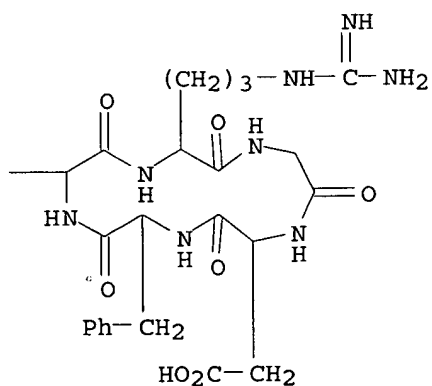
CM 1

CRN 250612-47-6
 CMF C59 H87 N19 O16

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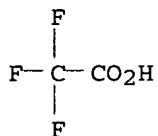


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CM 2

CRN 76-05-1
CMF C2 H F3 O2

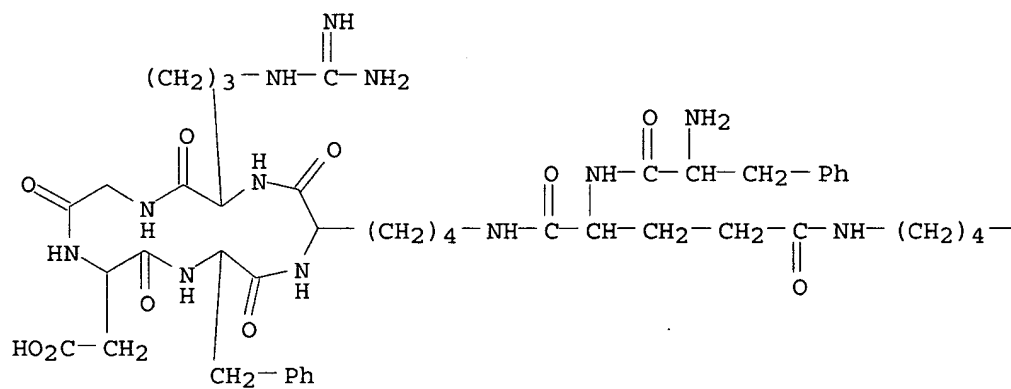


RN 250612-50-1 HCAPLUS
CN Cyclo(L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-L-lysyl),
5,5'-(L-phenylalanyl-L-glutamoyl)bis-, tris(trifluoroacetate) (9CI) (CA
INDEX NAME)

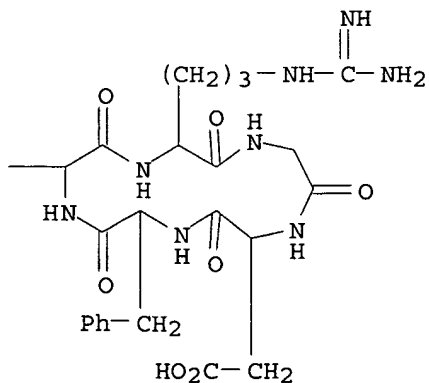
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CRN 250612-49-8
CMF C68 H96 N20 O17

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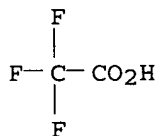


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CM 2

CRN 76-05-1
 CMF C2 H F3 O2

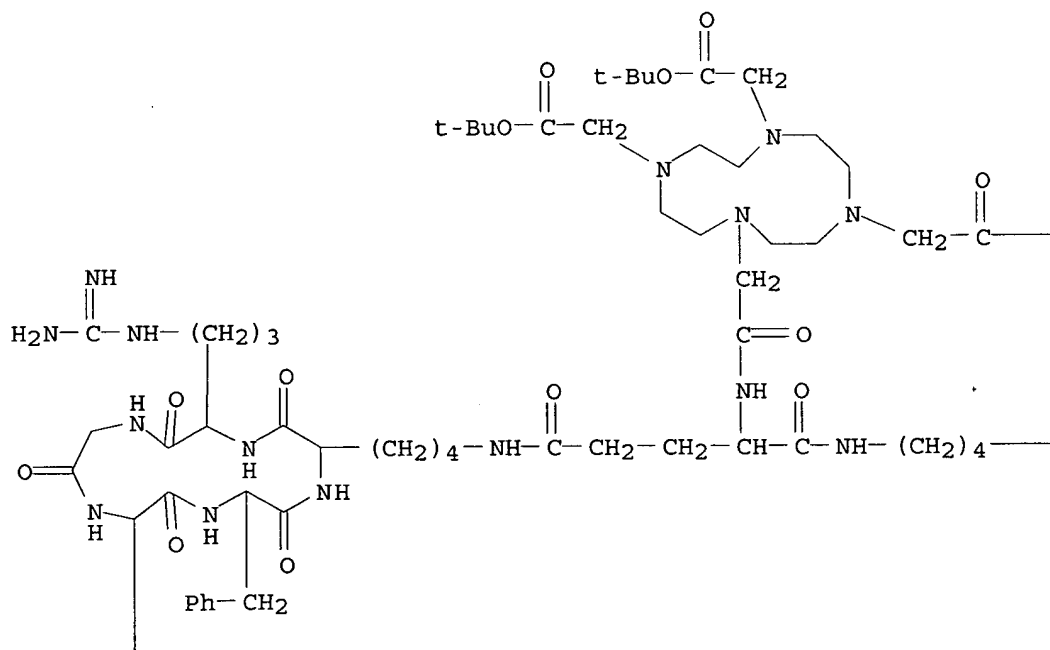


RN 250612-82-9 HCAPLUS
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 (9CI) (CA INDEX NAME)

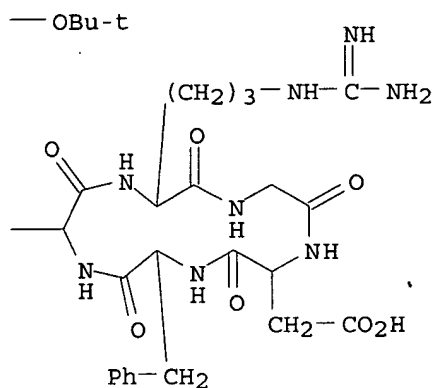
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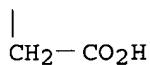
PAGE 1-A



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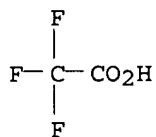
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CM 2

CRN 76-05-1

CMF C2 H F3 O2



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ACCESSION NUMBER: 2000:641663 HCAPLUS

DOCUMENT NUMBER: 134:9299

TITLE: Surface coating with cyclic RGD peptides stimulates osteoblast adhesion and proliferation as well as bone formation

AUTHOR(S): Kantlehner, Martin; Schaffner, Patricia; Finsinger, Dirk; Meyer, Jorg; Jonczyk, Alfred; Diefenbach, Beate; Nies, Berthold; Holzemann, Gunter; Goodman, Simon L.; Kessler, Horst

CORPORATE SOURCE: Institut fur Organische Chemie und Biochemie
Technische Universitat Munchen, Garching, 85747,

SOURCE: Germany
ChemBioChem (2000), 1(2), 107-114
Published in: Angew. Chem., Int. Ed., 39(16)
CODEN: CBCHFX; ISSN: 1439-4227
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The physiol. inertness of synthetic implant materials often results in insufficient implant integration and limited acceptance of implants in tissues. After implantation the implant surface is often separated from the surrounding healthy and regenerating tissue, for example by a fibrous capsule. To avoid this host-vs.-**graft** reaction, a strong mech. contact between tissue and implant must be ensured. An enhanced contact between **graft** and the surrounding tissue can be provided by coating the implant with cell-adhesive mols. The highly active and $\alpha v \beta 3$ - and $\alpha v \beta 5$ - **integrin**-selective peptide c(-RGDfk-) (f = D-phenylalanine) was functionalized with various linker mols. containing an acrylamide end group by using the lysine side chain of c(-RGDfk-). The acrylamide group can be used to bind the peptide covalently to poly(Methacrylate) (PMMA) surfaces. The coated surfaces effectively bind to murine osteoblasts as well as human osteoblasts in vitro when a min. distance of 3.5 nm between surface and the constrained RGD sequence is provided. In contrast to osteoblasts in cell suspension, surface-bound osteoblasts show no apoptosis but proliferate by a factor of 10 over a 22 d period. Coating of inert implant surfaces with highly active and αv -selective peptides affords a marked improvement in osteoblast binding over current technologies. In vivo studies show that peptide-coated PMMA pellets implanted into the patella groove of rabbits are integrated into the regenerating bone tissue faster and more strongly than uncoated pellets.

CC 63-7 (Pharmaceuticals)

ST cyclic RGD peptide implant coating biocompatibility; **integrin**
cyclic peptide implant bone formation

IT Transplant and Transplantation
(host-vs.-**graft** reaction; surface coating with cyclic RGD peptides stimulates osteoblast adhesion and proliferation as well as bone formation)

IT **Integrins**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
($\alpha v \beta 3$; surface coating with cyclic RGD peptides stimulates osteoblast adhesion and proliferation as well as bone formation)

IT **Integrins**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
($\alpha v \beta 5$; surface coating with cyclic RGD peptides stimulates osteoblast adhesion and proliferation as well as bone formation)

IT 190072-28-7 226559-20-2 226559-21-3
226559-22-4 226559-23-5 226559-24-6
308085-42-9
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(surface coating with cyclic RGD peptides stimulates osteoblast adhesion and proliferation as well as bone formation)

IT 190072-28-7 226559-20-2 226559-21-3
226559-22-4 226559-23-5 226559-24-6
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(surface coating with cyclic RGD peptides stimulates osteoblast adhesion and proliferation as well as bone formation)

IT 190072-28-7 226559-20-2 226559-21-3
226559-22-4 226559-23-5 226559-24-6

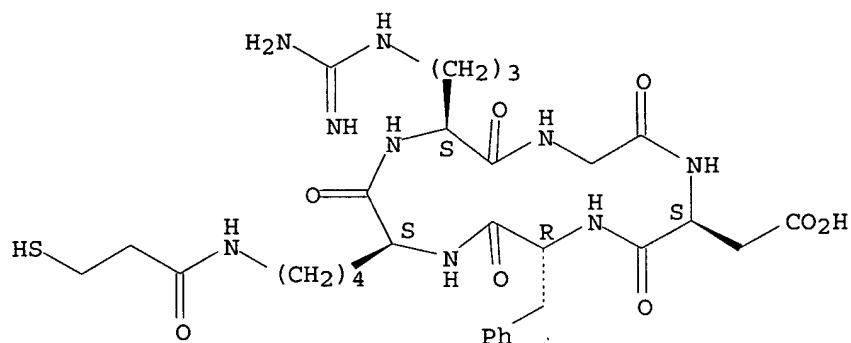
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(surface coating with cyclic RGD peptides stimulates osteoblast adhesion and proliferation as well as bone formation)

RN 190072-28-7 HCAPLUS

CN Cyclo[L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-N6-(3-mercapto-1-oxopropyl)-L-lysyl] (9CI) (CA INDEX NAME)

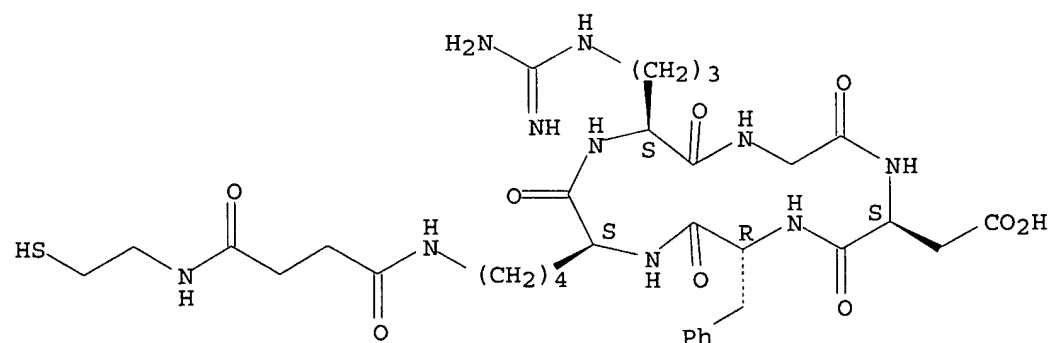
Absolute stereochemistry.



RN 226559-20-2 HCAPLUS

CN Cyclo[L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-N6-[4-[(2-mercaptoethyl)amino]-1,4-dioxobutyl]-L-lysyl] (9CI) (CA INDEX NAME)

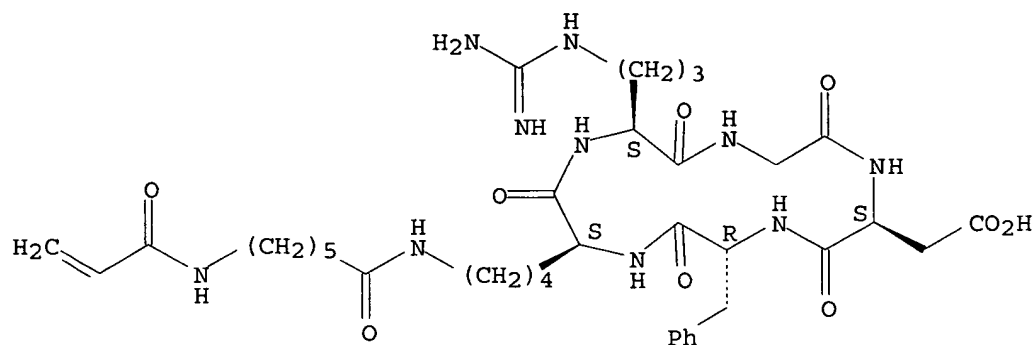
Absolute stereochemistry.



RN 226559-21-3 HCAPLUS

CN Cyclo[L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-N6-[1-oxo-6-[(1-oxo-2-propenyl)amino]hexyl]-L-lysyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.

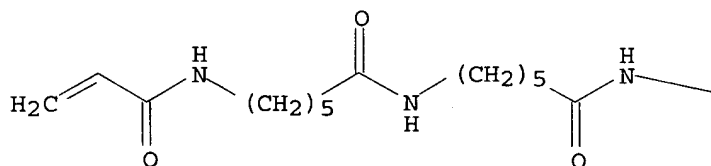


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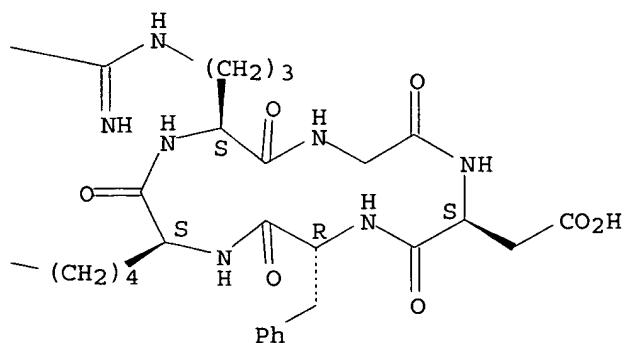
CN Cyclo[L-arginylglycyl-L-α-aspartyl-D-phenylalanyl-N6-[1-oxo-6-[[1-oxo-6-[(1-oxo-2-propenyl)amino]hexyl]amino]hexyl]-L-lysyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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H₂N—

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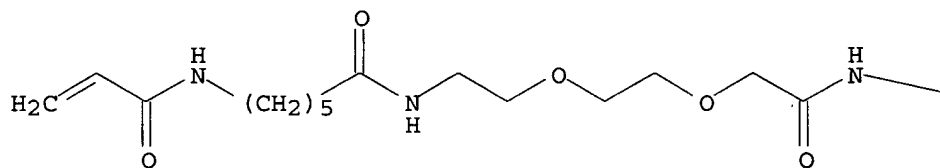
RN 226559-23-5 HCAPLUS

CN Cyclo[L-arginylglycyl-L-α-aspartyl-D-phenylalanyl-N6-(1,10,17-trioxo-3,6-dioxo-9,16-diazanonadec-18-en-1-yl)-L-lysyl] (9CI) (CA INDEX NAME)

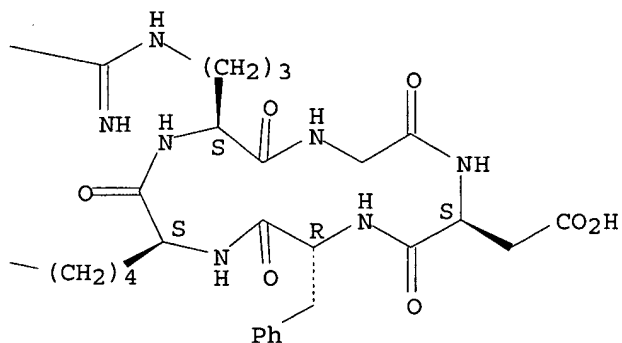
Absolute stereochemistry.

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H₂N—



PAGE 1-B

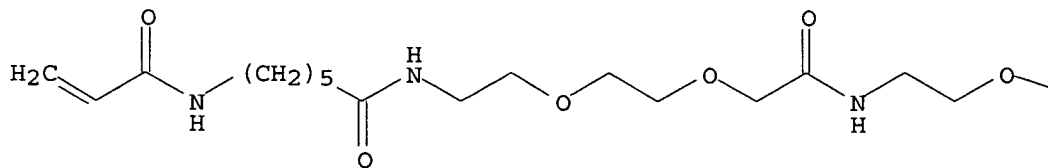


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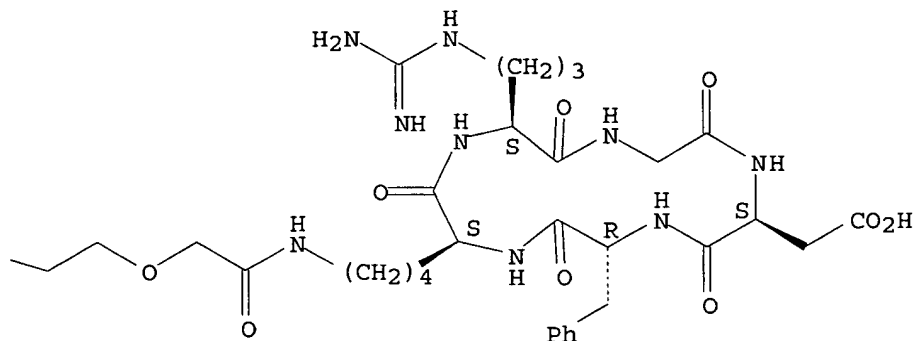
CN Cyclo[L-arginylglycyl-L-α-aspartyl-D-phenylalanyl-N6-(1,10,19,26-tetraoxo-3,6,12,15-tetraoxa-9,18,25-triazaoctacos-27-en-1-yl)-L-lysyl]
(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 41 OF 43 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:178367 HCAPLUS

DOCUMENT NUMBER: 130:342955

TITLE: Selective RGD-mediated adhesion of osteoblasts at surfaces of implants

AUTHOR(S): Kantlehner, Martin; Finsinger, Dirk; Meyer, Jorg; Schaffner, Patricia; Jonczyk, Alfred; Diefenbach, Beate; Nies, Berthold; Kessler, Horst

CORPORATE SOURCE: Institut fur Organische Chemie und Biochemie, Technischen Universitat Munchen, Garching, D-85747, Germany

SOURCE: Angewandte Chemie, International Edition (1999), 38(4), 560-562

CODEN: ACIEF5; ISSN: 1433-7851

PUBLISHER: Wiley-VCH Verlag GmbH

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A new optimized method for coating of implants using **integrin**-specific peptide ligands and the direct covalent anchoring of these peptides to the common **graft** material poly(Me methacrylate) (PMMA) is reported. These surfaces bind osteoblasts, stimulate their proliferation, and therefore trigger biol. tissue regeneration. The cyclic pentapeptide employed was c(-RGDfX-) (f = D-phenylalanine), which is selective for the $\alpha v \beta 3$ and the $\alpha v \beta 5$ **integrin** receptors. The X is a lysine residue which allows linkage of the peptide over a length-optimized spacer through an acrylic acid functional group to the PMMA **graft** used as a bone implant. The method demonstrates an attractive strategy for the development of cell-free and bioactive implants that carry the biol. information for the selective activation of target cells needed for selective tissue regeneration.

CC 63-7 (Pharmaceuticals)

IT 161552-03-0

RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(peptides containing; selective RGD-mediated adhesion of osteoblasts at surfaces of implants)

IT 161552-03-0

RL: BPR (Biological process); BSU (Biological study, unclassified); PEP

(Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(peptides containing; selective RGD-mediated adhesion of osteoblasts at surfaces of implants)

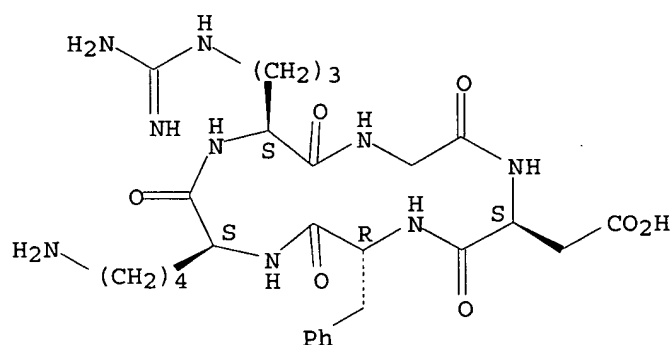
IT 161552-03-0

RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(peptides containing; selective RGD-mediated adhesion of osteoblasts at surfaces of implants)

RN 161552-03-0 HCAPLUS

CN Cyclo(L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-L-lysyl) (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L47 ANSWER 42 OF 43 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:463996 HCAPLUS

DOCUMENT NUMBER: 127:158602

TITLE: Two novel probes reveal tubular and vascular Arg-Gly-Asp (RGD) binding sites in the ischemic rat kidney

AUTHOR(S): Romanov, Victor; Noiri, Eisei; Czerwinski, Grzegorz; Finsinger, Dirk; Kessler, Horst; Goligorsky, Michael S.

CORPORATE SOURCE: State University of New York, Stony Brook, NY, USA

SOURCE: Kidney International (1997), 52(1), 93-102

CODEN: KDYIA5; ISSN: 0085-2538

PUBLISHER: Blackwell

DOCUMENT TYPE: Journal

LANGUAGE: English

AB We previously demonstrated that RGD peptides prevent tubular obstruction in ischemic acute renal failure (ARF) and suggested that exposed unoccupied **integrin** receptors represent the target for such therapy. The present study investigated the topog. of RGD binding sites and **integrin** receptors in ischemic rat kidneys. Two RGD peptides were synthesized: a cyclic biotinylated (Bt) RGD peptide and a linear RGD peptide (GRGDSP) labeled with rhodamine green (RhoG). Rats were subjected to 45 min of renal artery occlusion, kidneys were harvested at different times post-ischemia, and stained with RGD peptides and a panel of antibodies to **integrins**. In control, Bt-RGD staining was undetectable in alkaline phosphatase histochem., whereas immunofluorescence detection with Rho-streptavidin conjugate as well as

RhoG-GRGDSP staining faintly decorated the basolateral aspect of the **proximal** tubular cells in a punctate fashion. In contrast, ischemic kidneys showed binding to the basolateral and apical aspects of **proximal** tubules, peritubular capillaries, and desquamated cells within tubular lumen. The most conspicuous staining of ischemic kidneys was obtained with antibodies to the $\beta 1$ (labeling of the apical aspect of **proximal** and distal tubules, as well as desquamated cells obstructing tubular lumen) and the αV (glomeruli, tubular epithelia, intima of blood vessels stained faintly, while the obstructing cellular conglomerates showed intense staining) subunits. Double staining with Bt-RGD and antibodies against the $\beta 1$ and $\alpha V \beta 3$ **integrins** showed co-localization of staining within the tubules and vasculature, resp. In vitro attachment of HL-60 leukocytes to the endothelial cells was inhibited by the cyclic RGD peptide. In conclusion, expression of RGD binding sites and $\beta 1$ **integrin** subunits along the apical aspect of tubular epithelia and on the surface of desquamated cells is in concert with the hypothesis on the pathogenetic role of RGD-recognizing **integrins** in tubular obstruction. The expression of RGD binding sites along the intimal surface of blood vessels in ischemic kidneys suggests an addnl. target for RGD peptides in vascular endothelial cells.

CC 9-4 (Biochemical Methods)

Section cross-reference(s): 14

ST kidney ischemia RGD binding site staining; arginylglycylaspartate binding site kidney ischemia; immunol staining RGD binding site kidney;
integrin RGD recognition kidney tubule obstruction

IT **Integrins**

RL: ANT (Analyte); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
 (probes to reveal tubular and vascular Arg-Gly-Asp binding sites in ischemic kidney)

IT **Integrins**

RL: ANT (Analyte); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
 ($\beta 1$; probes to reveal tubular and vascular Arg-Gly-Asp binding sites in ischemic kidney)

IT **188982-05-0P**

RL: ARG (Analytical reagent use); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
 (probes to reveal tubular and vascular Arg-Gly-Asp binding sites in ischemic kidney)

IT **188982-05-0P**

RL: ARG (Analytical reagent use); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
 (probes to reveal tubular and vascular Arg-Gly-Asp binding sites in ischemic kidney)

IT **188982-05-0P**

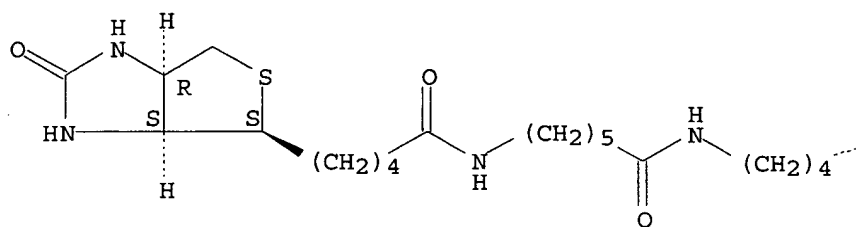
RL: ARG (Analytical reagent use); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
 (probes to reveal tubular and vascular Arg-Gly-Asp binding sites in ischemic kidney)

RN 188982-05-0 HCAPLUS

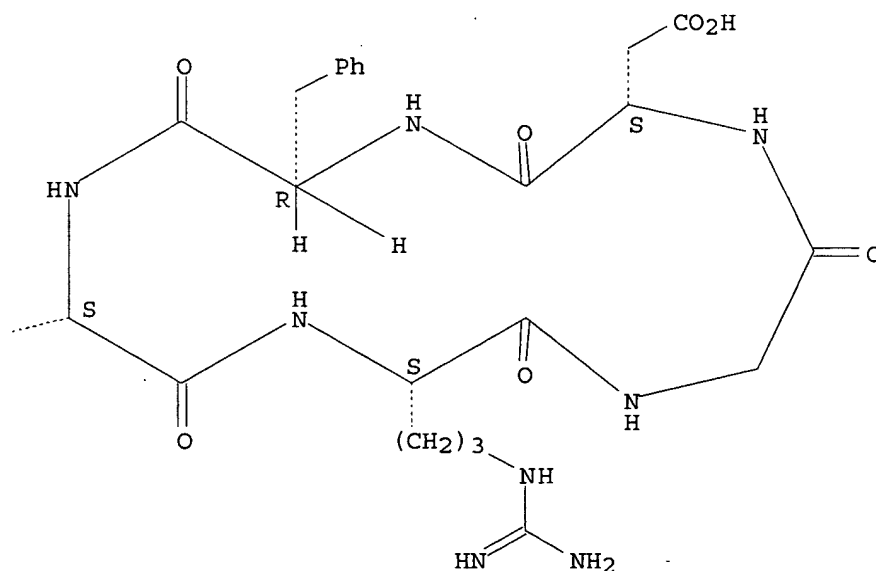
CN Cyclo[L-arginylglycyl-L- α -aspartyl-D-phenylalanyl-N6-[6-[[5-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-1-oxopentyl]amino]-1-oxohexyl]-L-lysyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L47 ANSWER 43 OF 43 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:998368 HCAPLUS

DOCUMENT NUMBER: 124:76558

TITLE: Method of enhancing wound healing by stimulating fibroblast and keratinocyte growth in vivo, utilizing amphipathic peptides

INVENTOR(S): Jaynes, Jesse M.; Julian, Gordon R.

PATENT ASSIGNEE(S): Demeter Biotechnologies, Ltd., USA

SOURCE: PCT Int. Appl., 64 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 11
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9528832	A1	19951102	WO 1995-US4718	19950419
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, UZ, VN				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5561107	A	19961001	US 1994-231730	19940420
AU 9522937	A1	19951116	AU 1995-22937	19950419
EP 756449	A1	19970205	EP 1995-916435	19950419
EP 756449	B1	20031119		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
AT 254396	E	20031215	AT 1995-916435	19950419
PRIORITY APPLN. INFO.:			US 1994-231730	A 19940420
			US 1993-39620	B2 19930604
			US 1993-148491	B2 19931108
			US 1993-148889	B2 19931108
			US 1994-225476	B2 19940408
			WO 1995-US4718	W 19950419
AB	A method of treating a wound of a mammalian subject in need of such treatment, to promote healing thereof, comprises administering to the subject, e.g., to the wound locus, a composition comprising a fibroblast and keratinocyte proliferatingly effect amount of an amphipathic peptide, preferably an amphipathic peptide which is antimicrobially effective at the locus. A method is also disclosed of stimulating the accelerated growth of dermal tissue in a tissue culture containing it, comprising applying to the tissue culture a fibroblast and keratinocyte proliferatingly effective amount of an amphipathic peptide, by which the dermal tissue may be grown to produce skin for skin grafting purposes, utilizing a dermal tissue culture containing dermal tissue material of a skin graft recipient of such skin. Novel amphipathic peptides suitable for use in such methods are disclosed.			
IC	ICM A01N001-02			
CC	ICS A61K038-10; A61K038-17; C07K007-08; C07K014-435; C12N005-08			
ST	1-12 (Pharmacology)			
IT	amphipathic peptide wound healing; fibroblast keratinocyte growth amphipathic peptide; skin graft tissue culture amphipathic peptide			
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	glyoxylated	162136-49-4	162136-49-4D, N-methylated or	
	glyoxylated	162136-51-8	162136-51-8D, N-methylated or	
	glyoxylated	162136-52-9	162136-52-9D, N-methylated or	
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 RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or
 effector, except adverse); BSU (Biological study, unclassified); THU
 (Therapeutic use); BIOL (Biological study); USES (Uses)

(amphipathic peptides for enhancing wound healing by stimulating
 fibroblast and keratinocyte growth in vivo)

IT 172212-29-2 172212-29-2D, N-methylated or glyoxylated
 RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or
 effector, except adverse); BSU (Biological study, unclassified); THU
 (Therapeutic use); BIOL (Biological study); USES (Uses)

(amphipathic peptides for enhancing wound healing by stimulating
 fibroblast and keratinocyte growth in vivo)

IT 172212-29-2 172212-29-2D, N-methylated or glyoxylated
 RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or
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 (Therapeutic use); BIOL (Biological study); USES (Uses)

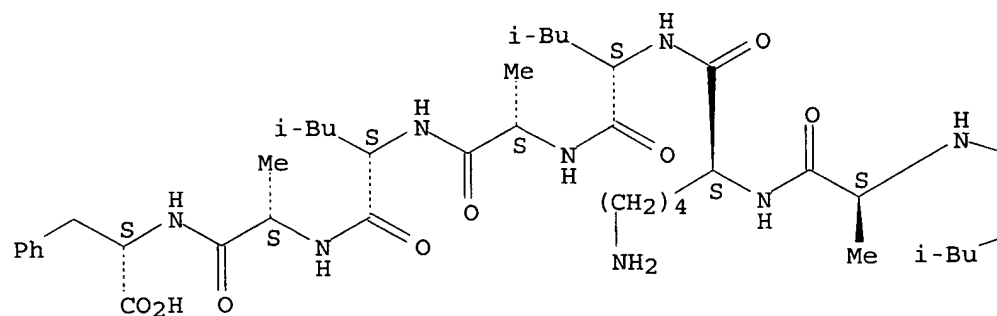
(amphipathic peptides for enhancing wound healing by stimulating
 fibroblast and keratinocyte growth in vivo)

RN 172212-29-2 HCAPLUS

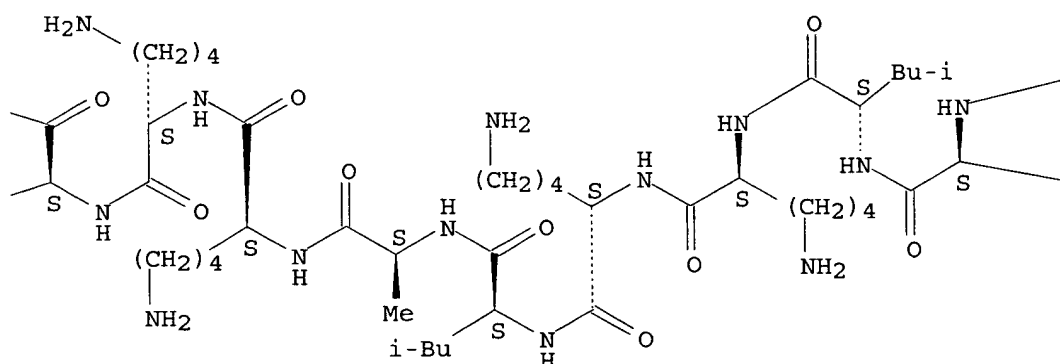
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 INDEX NAME)

Absolute stereochemistry.

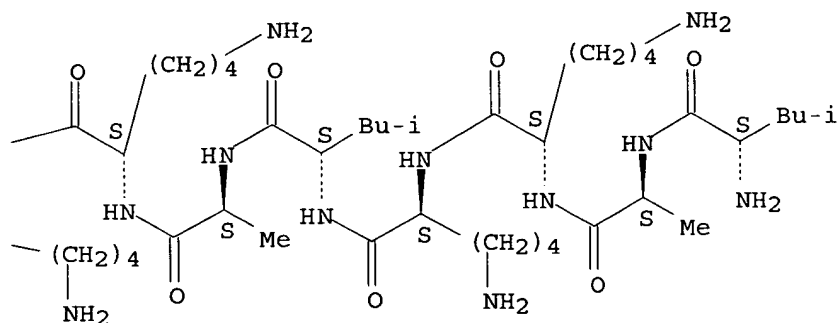
PAGE 1-A



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PAGE 1-C



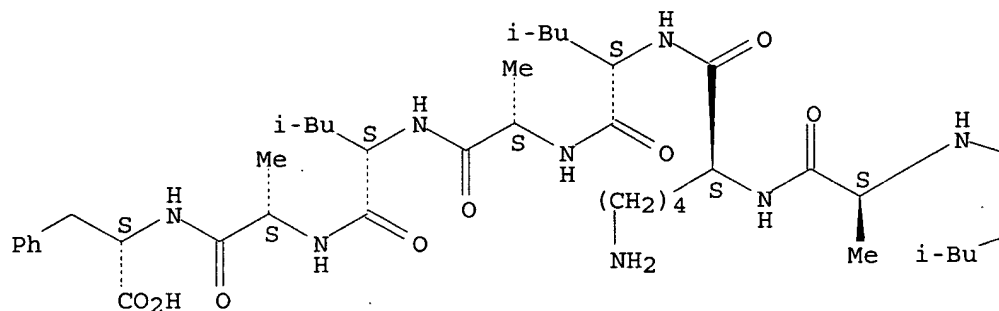
RN 172212-29-2 HCAPLUS

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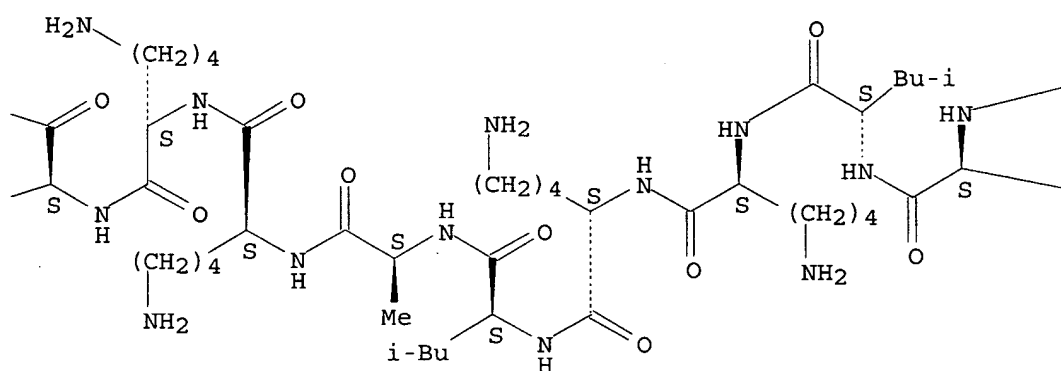
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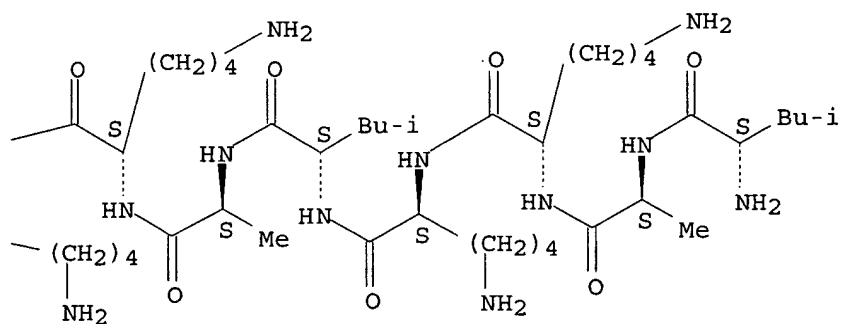
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